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LUMBAR APPROACH TO RENAL ARTERY FOR APPLICATION OF THE GOLDBLATT CLAMP

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When studies connected with the production of experimental hypertension were undertaken, work in this field was carefully considered and the method of Goldblatt adopted.[1] In brief, this consists of partially occluding the renal artery with a small metal clamp. By this method it is possible to produce in animals marked hypertension which persists for a long time. Dogs were chosen as the most suitable experimental animals, and Goldblatt clamps as originally designed were employed. In studying the method of application of the Goldblatt clamp, one of us (Glenn) felt that the clamp holder was not only unnecessary but unsurgical, as its use presupposed an approach larger than a successful application of the clamps warranted. Studies were therefore undertaken in an effort to devise a more suitable method. The results, as embodied in the following detailed operative procedure, are based on numerous postmortem dissections as well as on the successful production of experimental hypertension in many animals.

The basis for this approach is found in the fact that the renal artery lies posterior to the other structures of the renal pedicle. It is separated from the deep fascial and muscular structures of the back merely by perirenal fat. In thirty-two animals it has been found that on the right the renal artery lies at a level marked externally by the lower border of the last rib while on the left it lies about 2 cm. below this point. It is with these landmarks in mind that the incisions are made.

The animal is placed on its abdomen on the usual trough-shaped operating table. Beneath the abdomen several folded towels are placed. These towels steady the animal and displace the abdominal contents

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From the Department of Surgery of the New York Hospital and Cornell Medical College.

1. Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: J. Exper. Med. **59**:347, 1934.

dorsally. The skin of the back is clipped, shaved and sterilized with the usual iodine-alcohol technic. Sterile towels are applied to isolate the operative fields.

On the right side, the incision in the skin, 4 cm. long, is started about 2 cm. from the midline, running parallel to and along the lower border of the twelfth rib. This incision is carried down through the skin and subcutaneous tissue, and the lumbodorsal fascia is well exposed. This fascia is then incised throughout the length of the incision. At

The right renal artery and its bifurcation are shown. The artery is held forward at the point where the Goldblatt clamp is to be applied.

about the lower third of the incision the union of the fasciae of the internal and that of the external oblique muscle can be identified. The fascia of the internal oblique muscle must be incised, as its course inward and downward is followed. By blunt dissection the bundle of the thick longissimus dorsi muscle can be partially freed from its surrounding structures and retracted medially as a whole. This procedure leaves the tendinous origin of the transverse abdominal muscle exposed. This muscle forms the floor of the incision and the roof of the perirenal

space, and must then be incised in the course of its fibers and held apart, as shown in the illustration.

If the incision has been correctly placed, the perirenal fat behind the kidney is exposed. By insertion of the finger in the triangular space provided, the region of the right pedicle can be easily explored. Laterally the notch in the kidney representing the pedicle can be identified. Medially and dorsally the aorta is readily palpable. If the finger is swept longitudinally between these structures the renal artery can be identified as a strongly pulsating cord. By gentle outward retraction on the fat and blunt dissection the artery can easily be freed for a distance sufficient to allow the application of the clamp.

It has been found unnecessary to use the complicated clamp holder originally advised by Goldblatt. If the tray is removed and the clamp gripped in a small curved mosquito hemostat, the clamp can readily be passed beneath the artery and the tray replaced. As the tension is relieved, the clamp recedes within the perirenal fat, from which the head can readily be retrieved. The body of the clamp is then fixed with a pair of long forceps and tightened to the required degree. The wound is closed in layers with interrupted sutures of fine silk.

On the left side, there are no essential differences in the operative technic other than that the incision is made 2 cm. below the twelfth rib.

Goldblatt clamps have been applied bilaterally in a total of thirty-two dogs. For twenty-nine of these dogs, determinations of blood pressure have been made, and satisfactory hypertension was produced in twelve. Of the remaining seventeen animals, eight died because of too great a constriction of the arteries, five required a second operation to increase the constriction of the arteries and four required a second operation to diminish the constriction of the arteries.

Of the five animals in which the clamp was tightened, two died; satisfactory hypertension developed in the remaining three. Of the four animals in which the clamps were loosened, one died and the remaining three recovered, satisfactory hypertension later developing.

Thus, in twenty-nine animals, a level of hypertension satisfactory for further experimentation developed in eighteen.

EFFECT OF PASSING RENAL BLOOD THROUGH LIVER IN DOGS WITH EXPERIMENTAL HYPERTENSION

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For many years it has been recognized that the liver has as one of its functions a detoxifying action. It excretes certain heavy metals, dysentery toxin and ricin into the bile.[1] It has been shown that the injection of phenol, benzoic acid and phenoltetrachlorphthalein in amounts which normally produce no reaction may prove fatal in hepatectomized dogs.[1] It is known that in the absence of the liver amino acids injected into an animal are not destroyed.[2] Numerous observers have suggested that the liver protects the body from both endogenous and exogenous poisons. The liver takes up the bulk of chemical poisons, removes chloroform and phenol from the organism and protects it against the alkaloids. Most of these actions of the liver are based on the so-called glycuronic acid synthesis, whereby glycogen unites with these substances to form corresponding acids which are removed by the kidney. Many times the lethal dose of certain micro-organisms can be injected into the portal vein.[3]

As initially described by Goldblatt,[4] partial constriction of the renal artery, which produces ischemia in the kidney, results in a permanent hypertension in dogs [4] and monkeys.[5] There is the possibility that a substance is formed in the damaged kidney and carried in the blood stream that is responsible for the elevated blood pressure. As yet no such substance has been demonstrated in the blood stream either by

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1. Wright, Samson: Applied Physiology, ed. 6, New York, Oxford University Press, 1936, p. 490.

2. Wright,[1] p. 489.

3. Rolleston, H., and McNee, J. W.: Diseases of the Liver, Gallbladder and Bile Ducts, ed. 3, New York, The Macmillan Company, 1929, p. 18.

4. Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: J. Exper. Med. **59**:347, 1934.

5. Goldblatt, H.: Am. J. Path. **12**:760, 1936.

direct transfusion [6] or by extraction of plasma.[7] It has been stated by some observers that extracts of ischemic kidneys have greater pressor effect than extracts of normal kidneys.[8]

In view of the possibility of the formation of a pressor substance in the ischemic kidney and the further possibility that this substance might be modified or destroyed by passage through the liver, it seemed of interest to determine the effect in experimental hypertension of the direct passage of blood from the ischemic kidney through the liver.

METHOD

The venous flow from the kidney was shunted directly through the liver by way of the inferior vena cava and the portal vein. This was accomplished by anastomosing the inferior vena cava above the entrance of the renal veins to the portal vein and ligating the former on the cardiac side of the stoma. As a result of this procedure the venous blood from the kidneys passed directly through the liver. Hypertension had been previously produced by the method of Goldblatt,[4] and the systolic blood pressure had been measured by the carotid loop method, originally described by van Leersum. For estimation of the blood pressure five readings were made one minute apart and the lowest of these charted as the pressure for the day.

The protocols of four experiments are given. In the first two experiments the fistula between the inferior vena cava and the portal vein was established before hypertension was produced; in the last two experiments the hypertension was produced before the fistula between the inferior vena cava and the portal vein was established.

EXPERIMENTAL DATA

EXPERIMENT 1.—*(a) Carotid loop, (b) reverse Eck fistula and (c) application of Goldblatt clamps to the renal arteries.*

On Aug. 13, 1936, with the animal under anesthesia induced by intravenous injection of pentobarbital sodium, a van Leersum carotid loop was made in a healthy police dog which weighed 34 pounds (15.5 Kg.). The postoperative course was marred by an infection in and about the loop, but the wound finally healed satisfactorily. On the eleventh postoperative day, determinations of blood pressure were started. Daily readings of the blood pressure were made for eighty days, during which time fifty readings were taken. The normal blood pressure of the dog was found to be about 140 mm. of mercury.

On Nov. 11, with the same type of anesthesia, the inferior vena cava was anastomosed to the portal vein, a window approximately 2.5 by 1 cm. being formed between the two vessels. After the anastomosis was demonstrated to be patent, the vena cava was ligated above the fistula, and there followed immediately a marked engorgement of the mesenteric vessels. A definite increase in the size of the portal vein on the hepatic side of the fistula was observed, and it was felt that the liver itself increased somewhat in size. The animal recovered

6. Collins, D. A., and Hoffbauer, F. W.: Proc. Soc. Exper. Biol. & Med. **35**: 539, 1937.

7. Page, I. H.: Proc. Soc. Exper. Biol. & Med. **35**:112, 1936.

8. Prinzmetal, M., and Friedman, B.: Proc. Soc. Exper. Biol. & Med. **35**:122, 1936. Harrison, T. R.; Blalock, A., and Mason, M. F.: ibid. **35**:38, 1936.

promptly from the anesthesia and seemed to be little disturbed by the procedure. The wound healed by first intention. For the following ten days the readings of the dog's blood pressure were 120, 120, 135, 140, 160, 160, 140, 170 and 140 mm. of mercury.

On November 21, Goldblatt clamps were applied to both renal arteries, and a degree of constriction was produced to occlude approximately 75 per cent of the normal flow of blood. The animal seemed little disturbed by the procedure; it recovered promptly from the anesthesia. Both wounds healed by first intention. During the next four weeks the blood pressure rose slowly but steadily and reached a level between 200 and 220 mm. of mercury. It has remained at this elevated level for ten weeks, and the animal is alive and well with a definite and persistent hypertension at the time of writing, March 15, 1937.

EXPERIMENT 2.—(*a*) *Reverse Eck fistula,* (*b*) *carotid loop and* (*c*) *application of Goldblatt clamps to the renal arteries.*

On Oct. 24, 1936, with the animal under anesthesia induced by intravenous injection of pentobarbital sodium, the inferior vena cava and portal veins were exposed in a healthy male dog, which weighed 28 pounds (12.7 Kg.), and an anastomosis was made between the two vessels. The vena cava was ligated just cephalad to the fistula. The animal withstood this procedure well and recovered promptly from the anesthesia. The wound healed by first intention. The postoperative course was uneventful save that for several days after the operation the animal exhibited moderate edema of the penis, scrotum and lower extremities. This edema disappeared within a few days.

On November 6, a van Leersum carotid loop was made in the animal's neck while it was under pentobarbital sodium anesthesia. The wounds healed slowly because of a marked secondary infection, but by the seventeenth postoperative day satisfactory determinations of blood pressure could be made. These determinations were made daily from November 23 to December 13 and showed a level of approximately 150 to 160 mm. of mercury.

On December 14, with the dog under pentobarbital sodium anesthesia, Goldblatt clamps were applied to the renal arteries. The recovery was uneventful, and both wounds healed by first intention. The blood pressure rose sharply to a level of 200 mm. of mercury within a week. By the fourth postoperative week the blood pressure had risen to a level of from 220 to 240 mm. of mercury. This level of pressure was maintained for more than six weeks. At the time of writing, March 15, 1937, the animal is alive and well, with a blood pressure of 230 to 240 mm. of mercury.

EXPERIMENT 3.—(*a*) *Carotid loop,* (*b*) *application of Goldblatt clamps to the renal arteries and* (*c*) *reverse Eck fistula.*

On Sept. 10, 1936, with the animal under anesthesia induced by intravenous injection of pentobarbital sodium a van Leersum carotid loop was made in the neck of a healthy young male dog which weighed 17½ pounds (7.9 Kg.). The wounds healed slowly because of secondary infection, and it was not until the eleventh postoperative day that determinations of blood pressure could be started. In order to establish a normal level, twenty-five readings were taken over a period of one month.

On October 23, Goldblatt clamps were applied to the renal arteries with the dog under pentobarbital sodium anesthesia. Within three days the blood pressure had risen to 190, but in the course of the next ten weeks it fell to approximately 160 to 170 mm. of mercury. This was not considered to be a satisfactory level of hypertension for experimental purposes; so the clamps were reexplored on Jan. 5, 1937,

and each one was tightened one-half turn. After this procedure, the blood pressure rose to about 200 mm. of mercury, where it persisted for seven weeks.

On February 20, with the dog under pentobarbital sodium anesthesia the inferior vena cava and the portal veins were exposed and anastomosed above the entrance of the renal veins. After the patency of the anastomosis was demonstrated, the inferior vena cava was ligated above the point of communication between the two veins. As is usually observed, the mesenteric vessels and the portal vein became engorged. The liver, however, did not increase appreciably in size. On the first day after operation the pressure rose to 260 mm. of mercury, but by the third postoperative day it had regained its preoperative level, of 200 mm. of mercury. At the time of writing, March 15, 1937, three weeks after the last operation, the animal is alive and well without evidence of change in the level of hypertension.

EXPERIMENT 4.—(*a*) *Carotid loop,* (*b*) *application of Goldblatt clamps to the renal arteries and* (*c*) *reverse Eck fistula.*

On Nov. 7, 1936, with the animal under anesthesia induced by intravenous injection of pentobarbital sodium, a van Leersum carotid loop was made on the neck of a healthy male dog which weighed 21 pounds (9.5 Kg.). Within ten days the loop had healed so satisfactorily that determinations of blood pressure could be made. These determinations were made over a period of twenty-four days and showed a normal pressure of 160 to 170 mm. of mercury.

On December 10, Goldblatt clamps were applied to both renal arteries under pentobarbital sodium anesthesia. Within three days the blood pressure had risen to about 260 mm. of mercury, but during the next twenty-six days fell slightly, establishing itself in the neighborhood of 230 mm. of mercury.

On Jan. 15, 1937, with the animal under open ether anesthesia, the inferior vena cava was anastomosed to the portal vein just above the entrance of the renal veins. After the anastomosis was demonstrated to be patent, the vena cava was ligated above the fistula. After this procedure there was the usual dilatation of the mesenteric and portal veins, but the liver was not noted to increase in size. The animal withstood this procedure well, and the wound healed by primary intention. Determinations of blood pressure were made frequently after operation; one hour after operation it was 140, twelve hours after operation it was 145 and twenty-four hours after operation it was 200 mm. of mercury. On the third postoperative day the blood pressure was 220. Before operation the urea nitrogen content of the blood was 18.6 mg. per hundred cubic centimeters and the sugar content 138 mg. On the third postoperative day the urea nitrogen content was 25.6 mg. and the sugar content 125 mg. On the seventh postoperative day the urea nitrogen content was 24.8 mg. and the sugar content 115 mg. On the twenty-seventh postoperative day the urea nitrogen content had fallen to 19.5 mg.

As noted, this animal's blood pressure returned to its level of hypertension of about 220 within three days. There it remained for the succeeding six weeks. At the time of writing, March 15, 1937, the animal is alive and well, without the hypertension's having been affected by shunting the venous flow through the liver.

COMMENT

In two experiments the reverse Eck fistula between the vena cava and the portal vein was established before hypertension was produced, and in two experiments hypertension was produced before the Eck fistula was established. By means of the ligation of the vena cava above the fistula in each instance, the blood returning from the kidneys

was shunted through the liver. In all four experiments the findings were essentially the same. In experiment 4 the urea nitrogen content of the blood was studied and was found to be slightly elevated for several days after operation. No explanation can be given for this, unless the renal function temporarily was impaired by back venous pressure. The experiments described indicate that the passage of the venous blood of the kidneys directly through the liver does not prevent the production of experimental hypertension in dogs, nor does it affect hypertension which has already been produced.

MODIFICATION OF VAN LEERSUM CAROTID LOOP FOR DETERMINATION OF SYSTOLIC BLOOD PRESSURE IN DOGS

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Many times in experimental work on laboratory animals there is a definite need for a satisfactory method whereby determinations of blood pressure can be made over a long period. The van Leersum carotid loop meets many of the requirements for a satisfactory method, but in its construction it is associated with a high morbidity and mortality. For this reason we became interested in attempting to devise an operative procedure and postoperative course which would make this operation more successful. The purpose, therefore, of this paper is to describe in detail the choice and preparation of the animals, the operative technic and the postoperative care associated with the construction of the so-called van Leersum carotid loop in dogs.[1]

The size and the age of the animal are of little importance in the ultimate success of the procedure, although in young and extremely active dogs it has been far more difficult to maintain a reasonable postoperative immobility. The activity of the dog subjects the loop to a higher incidence of infection, which results in a prolonged period of healing. It has been found that in animals with a great amount of loose skin on the ventral aspect of the neck the wound can be closed under less tension. This is considered a distinct advantage.

The neck of the animal selected for operation should be free from disease of the skin, such as the common sarcoptic mange, for the papules of the mites are invariably secondarily infected. The preparation of the skin is of importance. The heavy fur should be clipped carefully well beyond the operative site. Instead of shaving the skin at the operative site, it is further clipped, a Schick dry shaver being used to great advantage, though the fine clipper used on cats and rabbits probably would serve as well. It has been our experience that it is almost impossible to shave the neck of the animal without abrading the skin. From the

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1. van Leersum, E. C.: Arch. f. d. ges. Physiol. **142**:377, 1911.

minute abrasions there is sufficient exudation of lymph to provide an ideal culture medium in which the various bacteria present on the skin can grow luxuriantly. This in turn results in sufficient edema to cause actual pressure necrosis of the loop early in the postoperative course. On the other hand, it is not felt that the minute stubble left by clippers hinders sterilization of the skin by the usual benzine, ether-iodine-alcohol technic.

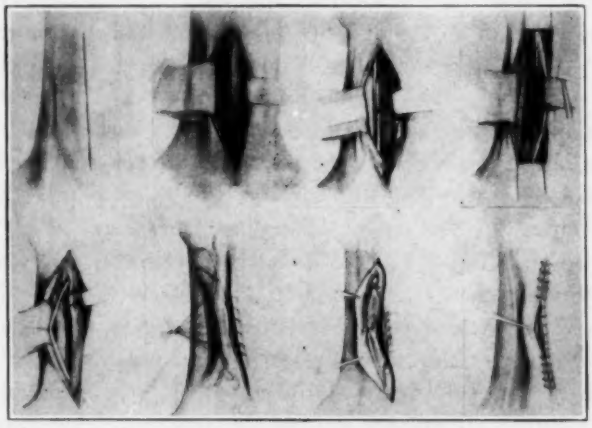
The animal is next transferred and securely strapped to the operating table. Two folded towels placed beneath the neck are adequate to aid in exposure and will not place too great a tension on the artery during the course of its isolation. The skin of the operative field is scrubbed with soft soap after it has been freed of fat with benzine; it is then washed with alcohol and ether. The skin is painted once with 7 per cent tincture of iodine, which is allowed to oxidize and then is removed with alcohol. A field large enough to permit the incision shown in the illustration is draped with sterile towels, and the rest of the animal is covered with the usual laparotomy sheet.

Emphasis should be placed on the careful planning of the incisions in the skin that are to form the loop. The midportion of the flap must lie directly over the carotid artery. By palpation the course of the artery is outlined along the tracheal border. With this course as the midline of the proposed flap, about 2 cm. of skin is taken on each side, this marking the width of the flap. The medial incision is then made slightly above the thyroid cartilage and is extended caudad to a point about 1 cm. lateral and 1 cm. above the manubrium sterni. In running parallel to the artery, the course of this incision is slightly diagonal across the trachea. The lateral incision again lies about 2 cm. from the line of the carotid artery and parallel to it. Instead, however, of being equal in length to the medial incision, the lateral incision is only half as long and lies opposite the midhalf of the former, as shown in the illustration. It has been customary to make this lateral incision equal in length to the midline incision. There is no need for this extra length, however, and it is a great hazard to the successful healing of the loop because it materially decreases the blood supply of the cutaneous flap. Also, in the final suturing of the artery within the flap the shorter incision leaves a junction of three free edges rather than four.

After the incisions are outlined, they are carried down through the skin to the subcutaneous tissues over the platysma myoides muscle. It is in the plane between the skin and that muscle that the flap is undermined. Though this procedure may seem to leave the skin without adequate blood supply, necrosis has never been observed. On the other hand, a flap so cut bears no tissue which may become edematous and cause subsequent necrosis owing to intrinsic pressure. With the blade of the knife held at an oblique angle, the skin is under-

mined throughout the course of the two incisions. All bleeding points are carefully clamped and tied with fine silk. The flap is then protected and held out of the field by a sponge saturated with saline solution, as shown in the illustration.

The subcutaneous tissue, the platysma myoides muscle and the anterior fascia of the neck are incised in the course of the midline incision down to the plane of cleavage between the sternohyoid and the sternomastoid muscle. By blunt dissection these muscles may be readily separated, disclosing at their depth the neurovascular bundle over which lies the internal jugular vein. The floor of the space so isolated is formed by the longus capitis muscle. By careful dissection, these muscles are separated at least 1 cm. above and below the limits of the incision in the skin. A landmark at this point is the superior thyroid artery,



The steps in the operative procedure in the order in which they are carried out.

which marks the uppermost portion of the carotid artery suitable for exteriorization. The plane of cleavage is followed caudad to the origin of the sternocleidomastoid muscle at the manubrium sterni. Throughout the limits of this incision the artery is first dissected free from the internal jugular vein and then from the vagus nerve. Traction is again obtained by means of a sponge wet with saline solution, as shown in the fourth section of the illustration.

The first stage in the exteriorization of the artery is that of reapproximation of the muscle borders beneath the vessel. This is accomplished with interrupted on end mattress sutures of medium silk, as shown in the illustration. The sutures at the extremities of the suture line must be placed carefully, leaving an opening sufficiently wide to insure free passage of the artery. In order to prevent tension on the completed loop due to contraction of the sternomastoid and sternohyoid muscles, it is important to reapproximate these muscles throughout

their course. At this point the artery may be included in the skin and temporarily held there by two short lengths of hernia tape, as shown in the sixth section of the illustration. This procedure readily permits placing the row of on end mattress sutures which are to hold the cutaneous edges of the neck. As this line is always subjected to a fair degree of tension, the use of on end mattress sutures is considered important, for it is the only suture which not only will act as a tension suture but will permit accurate approximation of the edges of skin. This suture also serves to bring the platysmal muscle and the subcutaneous tissues close together. In order to insure the evenness of this portion of the closure, it has been found advantageous to place this entire row of sutures before attempting to tie any of them. It is the midhalf of the medial incision which, of course, is approximated to the lateral. After their placement, the sutures are drawn taut and tied. They should be tight enough to secure adequate approximation of the edges of skin, but not tight enough to cause strangulation of the tissue.

The cutaneous flap will then be found to evert of its own accord toward the lateral aspect of the neck. The artery can easily be made to lie in the midportion of the flap. It is at this point that the most important suture in the entire procedure is placed. With the artery lying deep in the flap, a continuous suture of fine silk is started at the place where the vessel emerges from the muscle borders. The suture is so placed as to include the artery in a sling of skin which starts well above the junction of the three lines of suture and which will isolate the vessel from the line of suture of the under-side of the completed loop. These steps are well shown in the illustration. The importance of placing the artery deep within its flap rests on the following observation. About four days after operation, the cutaneous suture lines become infected. When the artery is allowed to rest directly on the line of cutaneous closure of the under-side of the loop, this inflammatory process spreads rapidly to the wall of the artery, weakening it sufficiently to allow erosion and subsequent fatal hemorrhage. When, however, the artery is protected by an intervening line of subcuticular tissue, hemorrhage has never been observed.

The last steps are relatively simple. As shown in the illustration, the proximal and distal quarters of the flap are closed with Staige-Davis sutures of medium silk, while the skin tube is closed with a continuous suture of the same material. This suture is started and finished as a purse-string, uniting all four edges of skin at their points of junction. This suture is placed intracutaneously.

The type of dressing is of importance. One thickness of gauze is placed beneath the loop. Along each border is placed a strip of gauze 4 by 4 inches (10 by 10 cm.), rolled in such a fashion as to relieve

partially the pressure caused by the remainder of the dressings. Around the neck is wrapped a gauze bandage several turns of which have been passed behind the forelimbs in order to prevent the dressing from riding upward on the animal's neck. Over this is placed a single plaster roll. Thus a secure dressing is provided which will adequately protect the loop from the animal's most persistent efforts at scratching. This initial dressing is not removed until the fifth postoperative day, at which time primary union is found to have taken place and the sutures of the upper and lower quarters are cut as well as the alternate ones of the middle half. A similar dressing is reapplied, except that the plaster is replaced by wide strips of adhesive tape. On the seventh postoperative day the dressing is again taken off and the sutures previously cut are removed, as are the remainder of the sutures in the middle half. At this time it will usually be found that the continuous suture on the under-side of the loop can easily be removed. The bandage may be replaced by a permanent collar of sufficient width to protect the loop from injury due to scratching by the animal. Although determinations of blood pressure have been started as early as the sixth day after operation, it is best to wait until the eighth or ninth day, by which time the last of the edema which is usually present has disappeared.

The results of this modification in the technic of making the van Leersum carotid loop have been satisfactory. Before the modification was developed, twenty-five of sixty-one animals survived and had satisfactory loops, the period between operation and determinations of blood pressure averaging eighteen and six-tenths days. Since the adoption of this modification, sixty-one dogs have been subjected to operation with one fatality and with satisfactory loops in the remainder. The interval between operation and determination of blood pressure has been reduced to an average of ten days.

ARTHROPLASTY OF THE HIP

A STATISTICAL STUDY OF SIXTY OPERATIONS

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There was used for this study a series of fifty-seven patients on whom arthroplasty of the hip was performed for various causes; three of the patients underwent bilateral arthroplasty, making a total of sixty operations. Included in the study were the age range, the types and variations of operative technic, the range of motion, the time elapsed since operation, the persistence of pain, the type of mobilization and the patient's personal reaction to the value of the operation regarding motion, pain and ability to get around and carry on his work.

Questionnaires were sent to all of these patients, and from these their personal reactions were obtained. From a clinical standpoint, several of the results which were classified as fair would have been classified as poor had not the personal reaction of the patient been taken into consideration.

RESULTS OF STUDY*

To classify the results, the following criteria were used. The operation was considered a failure when the patient had considerable pain or when complete, or almost complete, ankylosis resulted. The results were classified as good when there was at least 45 degrees of flexion and no pain and the patient was able to walk at least one-half mile (804 meters) without pain. The results were classified as fair when there was less than 45 degrees but more than 20 degrees of motion and the patient had little or no pain and was personally well satisfied with the result, either because of decreased pain, increased motion or better position of the limb. Several patients expressed satisfaction in spite of ankylosis because of decreased pain and betterment of position. In such cases the operation has been considered a failure.

It was noted, especially in the cases of hypertrophic arthritis, that pain was almost constantly present for from twelve to fourteen months. After this time the pain decreased markedly, and in some of the cases in which the results appeared to be fair or poor because of pain the actual end-results were good.

The classification of results according to the condition for which arthroplasty was done is found in table 1. It will be noted that there

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is a lower percentage of failures in those cases in which arthroplasty was done for hypertrophic arthritis than in those in which it was done for atrophic arthritis. There were no failures in those cases in which the operation was done for osteomyelitis. A high percentage (44.4 per cent) of good results was obtained in the cases of suppurative arthritis. This might lead one to believe that those conditions in which sclerosis of the bone is present would be more favorable for arthroplasty than infective or atropic arthritis, with the exception of gonorrheal arthritis, in case of which there is a relative, high percentage of good results (75 per cent in the present series).

There were three cases of congenital dislocation of the hip, in all of which the operative results were poor. There was no difference in the technic used in these cases. The fact that the acetabula were shallow is not the all important issue in these particular cases. One patient, in

TABLE 1.—*Classification of End-Results According to Pathologic Conditions*

Diagnosis	Bilateral Arthroplasty	No. of Arthroplasties	Good Results		Fair Results		Failure	
			No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Hypertrophic arthritis	1	15	7	46.66	6	40.0	2	13.33
Atrophic arthritis	2	21	4	19.5	8	38.09	9	42.85
Suppurative arthritis	0	9	4	44.4	3	33.3	2	22.2
Slipped epiphysis	0	4	1	25.0	2	50.0	1	25.0
Congenital dislocation	0	3	0	0.0	0	0.0	3	100.0
Osteomyelitis	0	3	1	33.3	2	66.6	0	0.0
Aseptic necrosis	0	1	1	100.0	0	0.0	0	0.0
Gonorrheal arthritis	0	4	3	75.0	0	0.0	1	25.0
Total cases	3	60	21	35.0	21	35.0	18	30.0

addition to having a shallow acetabulum, contracted pneumonia eight weeks after operation. Although the early motion was splendid, after the illness all motion was lost. The second patient, aged 10 years, was found to have an hour-glass contraction of the capsule with fat in the acetabulum. Besides reaming out the socket, a good shelf was built. Ankylosis occurred rapidly, however, in a position of adduction. The third case was one in which ankylosis developed after a manipulative attempt at closed reduction. The head, neck and trochanter were found markedly bound down with dense adhesions. Part of the acetabular shelf was chiseled off to allow abduction. The hip promptly fused in flexion and external rotation, and a trochanteric osteotomy has since been done to allow the hip a semineutral position.

Three patients underwent bilateral arthroplasty. The first patient suffered from hypertrophic arthritis, having pain and limitation of motion. The first operation gave a good result, the joint being stable and painless and having quite good motion. The second operation was more painful, and marked limitation of motion resulted. In the second case in which bilateral arthroplasty was performed good results were

obtained on the side on which the first operation was done, but rapid ankylosis occurred on the other side. This case was one of atrophic arthritis. In the third case only fair results were obtained on each side. The patient could get around the house without much distress, but considerable pain and tiredness resulted from going out of the house a few steps.

In one patient who was operated on following suppurative arthritis ankylosis developed which was resistant to two manipulations, and a second arthroplasty was done. On reoperation it was thought that the acetabulum had been made too deep, and the rim was cut down. There was much interposed scar tissue where the fascia had been placed. After the second arthroplasty, suppuration occurred, but despite this a splendid result was obtained, with no pain and with good range of motion. In fact, the boy won the high school single tennis championship last season.

TABLE 2.—*Results of Arthroplasty Classified According to Age Groups*

Age at the Time of Operation	No. of Operations	Good Results		Fair Results		Failure	
		No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
0-13	4	0	0.00	3	75.00	1	25.00
14-20	12	5	41.66	3	25.00	4	33.33
21-30	20	10	50.00	6	30.00	4	20.00
31-40	7	1	14.28	1	14.28	5	71.42
41-50	10	2	20.00	5	50.00	3	30.00
51-60	7	3	42.85	3	42.85	1	14.28
Total cases	60	21	35.00	21	35.00	18	30.00

Nevertheless, the operative result has been listed as a failure because the boy had a persistently draining sinus, owing to which he was unable to go swimming. The first arthroplasty, which resulted in ankylosis, was done while he was only 15 and possibly before the metaphysis had closed.

With the possibility in mind of epiphysial activity affecting the end-results, the results were classified according to ages in table 2.

The head of the femur fuses about the fifteenth or sixteenth year, and in the four cases in which arthroplasty was done before this time not a single good result was obtained. The next group in which poor results were obtained was made up of patients from 30 to 50 years of age. This included most of the patients operated on for atrophic arthritis, so the average was lowered more probably by this than by any age difficulty.

Most of the patients with suppurative arthritis were operated on between 21 and 30 years of age. As good results followed operations performed for this causative agent, a high percentage of good results would be expected in this age group. This was found to be the case.

Likewise, the good results in the cases of hypertrophic arthritis helped out the average of good results in the group of patients from 50 to 60 years of age.

An analysis of the cases according to the postoperative observation time brings out the figures presented in table 3.

In the first place, the patients operated on during the last few months obtained rather poor results. It was noted, however, in talking to the patients, especially those suffering from hypertrophic arthritis, that many were discouraged and suffered much pain during the first year after operation. It also followed that there was a definite tendency for

TABLE 3.—*Results of Arthroplasty Classified According to Postoperative Observation*

Time Since Operation	No. of Operations	Good Results		Fair Results		Failure	
		No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
6 mo.-1 yr.	5	2	40.00	2	40.00	1	20.00
1-2 yr.	10	5	50.00	3	30.00	2	20.00
2-3 yr.	10	5	50.00	4	40.00	1	10.00
3-5 yr.	7	1	14.28	4	57.14	2	28.57
5-10 yr.	18	6	33.33	5	27.77	7	38.88
10-20 yr.	10	2	20.00	3	30.00	5	50.00
Average postoperative observation time.	60	21	35.00	21	35.00	18	30.00

TABLE 4.—*Results Classified According to Operative Technic*

Type of Interposed Tissue	Total Cases	Good Results		Fair Results		Failure	
		No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Fascia	53	20	37.73	17	32.07	16	30.19
Other tissues	7	1	14.28	4	57.11	2	28.56
Total cases	60	21	35.00	21	35.00	18	30.00

this disability to decrease around from twelve to fourteen months after operation.

Whereas there appears to be a definite tendency to fewer good results after three years, there is a good reason for this. All but three of the patients with atrophic arthritis were operated on over three years ago, with good results in only 19.5 per cent. Cases of this type would naturally lower the incidence of good results. During the age period of from 3 to 5 years there was a sharp decline in the percentage of good results. This is explainable on the basis of one case of suppurative arthritis and two cases of congenital dislocation in which operation was performed during this period. Two cases of atrophic arthritis accounted for the fair results obtained during the same period.

In fifty-two cases a single layer of fascia lata was placed over the newly constructed head and anchored by sutures through a drill hole. This gave the higher percentage of good results, namely, 38.46 per cent. In only one case was a double layer of fascia used, that is, one layer over the acetabulum and the other over the newly constructed head. Whereas one case is not enough on which to form an opinion, there may be a greater tendency for the formation of scar tissue following this method, as rapid ankylosis occurred in this case. If all cases in

TABLE 5.—*Analysis of Failures*

Basis of Arthroplasty	Failures, No. of Cases	Pain, No. of Cases	Limited Motion, No. of Cases	Limited Motion and Pain, No. of Cases	Persistent Sinuses, No. of Cases
Hypertrophic arthritis	2	1	0	1	0
Atrophic arthritis	9	0	8	1	0
Suppurative arthritis	2	0	1	0	1
Gonorrheal arthritis	1	0	1	0	0
Slipped epiphysis	1	1	0	0	0
Congenital dislocation	3	0	2	1	0
Osteomyelitis	0	0	0	0	0
Aseptic necrosis	0	0	0	0	0
Totals	18	2	12	3	1
Percentage	100%	11.0%	66.0%	16.5%	5.5%

TABLE 6.—*Analysis of Fair Results*

Basis of Arthroplasty	Fair Results, No. of Cases	Slight Pain, No. of Cases	Limited Motion, No. of Cases	Limited Motion and Pain, No. of Cases	Persistent Sinuses, No. of Cases
Hypertrophic arthritis	6	1	2	3	0
Atrophic arthritis	8	6	0	2	0
Suppurative arthritis	3	1	2	0	0
Gonorrheal arthritis	0	0	0	0	0
Slipped epiphysis	2	0	2	0	0
Congenital dislocation	0	0	0	0	0
Osteomyelitis	2	1	1	0	0
Aseptic necrosis	0	0	0	0	0
Totals	21	9	7	5	0
Percentage	100%	42.84%	33.32%	23.80%	

which fascia was used are considered in one group, as in table 4, good results were obtained in 37.73 per cent. The results in the few cases in which muscle and fat were used are not conclusive, although in those in which fat was employed there was not a single good result. The failures are not due to variations in operative technic.

In comparing tables 5 and 6, it will be noted that 42.84 per cent of the results were listed as fair because of slight pain, whereas 66 per cent of the failures were so classed because of ankylosis. There was a greater tendency to ankylosis in the atrophic type of arthritis. Pain was the predominating cause of fair results in cases of atrophic arthritis,

whereas ankylosis was the main cause of the failures. The definite tendency to ankylosis in cases of atrophic arthritis is further shown in a case in which the results were classed as a failure due to ankylosis and in which subsequent arthroplasties were performed on both the opposite knee and one elbow. Ankylosis promptly occurred at these sites.

In regard to the operative technic, the types of interposed tissues and the relative results have already been discussed. For the more recent cases, the Smith-Petersen incision has been used and arthroplasty has been carried out following the technic of Albee. By far the poorest results were obtained with the Murphy approach and technic. This cannot be entirely blamed on the technic, as it was employed early, at which time the operation was limited more or less to rheumatoid or infectious types of arthritis.

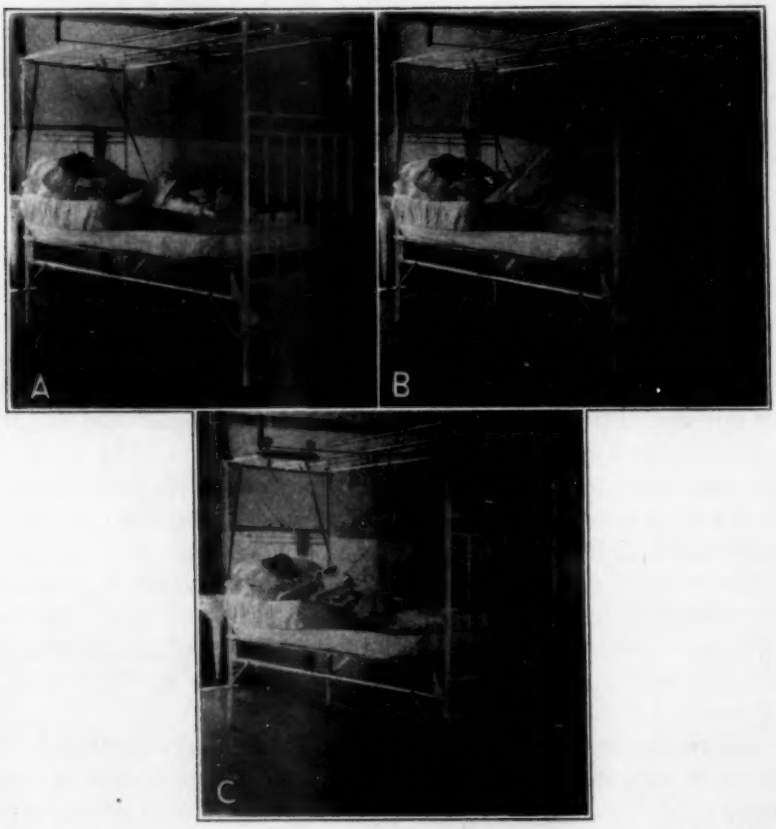
In all of the cases in which the Murphy type incision was used, the trochanter was chiseled off and replaced. This was not counted as altering the abductability of the leg. There were, however, fourteen cases in which the trochanter was either set down or wedged out. The results in these cases were as follows: good, three; fair, five, and failure, six. In four of the cases in which the trochanteric leverage was altered, the adductors were also sectioned. The results in two of these cases were fair and in two, poor. Apparently these procedures had no effect on the end-result in regard to stability and mobility. The adduction deformities were decreased, even in those cases in which the deformities existed prior to operation or in which a shallow acetabulum was found and increased abductability seemed advisable.

Postoperative manipulations were not of much value in increasing and maintaining motion. In two cases in which these were used fair results were obtained, and in one, failure resulted. Suppuration occurred in one case of osteomyelitis, accounting for the fair result in the group in which there were no failures.

Suppuration occurred in seven cases from the tenth to the twelfth day. This might indicate errors in operative technic. Suppuration occurred in three other cases after from four to six weeks. None of the operations for suppurative conditions were done until the condition had been quiescent for at least a year.

Postoperative treatment was quite uniform and consisted of immobilization in a cast or traction for from ten to fourteen days. This was followed by a gradual increasing of heat, massage and active and passive motion. Some form of traction was employed after the period of immobilization had ended. All patients were hospitalized and received physical therapy for two months after operation. They were then sent home on crutches but were definitely instructed not to bear weight for another two months. In the last seven cases a Patterson abduction

frame was used, as shown in the accompanying illustration. This consists of a frame, with a track overhead, so balanced that both active and passive abduction, flexion, internal rotation and traction can be obtained while the patient is in bed. This is used after the period of immobilization. Of those cases in which this apparatus was used good results were obtained in two and fair results in three, while two cases ended in fail-



Patterson's abduction frame. *A* shows the hip in extension but in a neutral position. In *B*, the extension is released while the patient passively or actively flexes the leg. In *C*, the extension is released while the leg is abducted. Note the hanger is at the extreme outer limit of the track.

ure. In one, failure was due to pneumonia, which developed after the patient was discharged from the hospital two months after operation. This necessitated a prolonged period without mobilization. In the second case, one of hypertrophic arthritis, suppuration occurred, and a sinus had to be resected twice. This prolonged the period of immobilization.

Since this study was made, arthroplasty has been done in two cases of traumatic dislocation of the hip and in two of atrophic arthritis. In one of the cases of atrophic arthritis a previous arthroplasty had been performed on the opposite hip with good results. The second case of atrophic arthritis was one in which complete ankylosis of both hips existed. Operation in these cases was done so recently that no attempt has been made to include them in this report.

SUMMARY

Uniformly poor results followed bilateral arthroplasties of the hip (three cases).

Results cannot be classified as failures merely because pain is present during the first year, as this is quite common, especially in cases of hypertrophic arthritis.

The best results were obtained in cases in which sclerotic bone existed, such as suppurative arthritis, osteomyelitis, hypertrophic arthritis and gonorrheal arthritis. The hardness of the bone may be an essential factor to a good end-result. Perhaps a synostosis could be considered as a good omen.

After mobilization has been started, a frame allowing active abduction and flexion while in traction has been of value.

Unsatisfactory results were obtained in cases in which operation was performed before epiphysial arrest occurred.

Atrophic arthritis and congenital dislocations were the basis of the highest percentage of unsatisfactory results.

The failures were not due to variations in operative technic.

Results on the whole are not dependent on the age of the patient but rather on the pathologic condition for which operation is performed.

HYGROMA COLLI CYSTICUM AND HYGROMA AXILLARE

PATHOLOGIC AND CLINICAL STUDY AND REPORT OF TWELVE CASES

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Hygroma, derived from the Greek *hygros* (moist) and *oma* (tumor), is a term which has often been used loosely to include various types of cysts containing a thin watery fluid. The designation cavernous lymphangioma has frequently been applied to the cystic form of this tumor. In a stricter sense, hygroma should be limited to multilocular cystic tumors of benign neoplastic nature which have a lymphatic origin and whose cavities are lined with true endothelium. These tumors originate, for the most part, in the neck and axilla and are then designated as hygroma colli cysticum and hygroma axillare. Occasional cases of hygroma occurring in the groin or in the retroperitoneal space have been reported.

Since these cystic tumors are relatively rare, the descriptions in the literature are limited in many instances to case reports, which are often incomplete, contradictory and unsupported by records of careful pathologic examination. The manner of growth and propagation of hygroma, its potentiality of increasing in size to an almost unlimited extent and its tendency to penetrate and destroy anatomic structures have heretofore been little understood. Because of the relatively obscure nature and the clinical importance of hygroma, this tumor deserved a careful and critical study to establish its pathologic nature and its manner of growth.

Opportunity was afforded to make gross and microscopic examinations in 12 cases of hygroma. As a result of these studies it has been possible to demonstrate the manner of growth and propagation of hygromatous cysts and thus to make clear this baffling problem. In addition to an account of the pathologic nature of hygroma, this report includes a critical clinical analysis of 12 cases of hygroma observed between 1925 and 1933 in the surgical departments of the Long Island College Hospital and the Long Island College of Medicine. Of the 12 hygromas studied, 10 occurred in the neck and 2 in the axilla. They comprised 1.2 per cent of the 981 tumors of all kinds, benign and

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malignant, exclusive of thyroid conditions, which occurred in the surgical service during the interval mentioned. I operated on 9 of the 12 patients and my colleagues on the remaining 3.

The first important contribution to the knowledge of hygroma was made by Wernher [1] in 1843. He recognized the favorite site of the tumor and demonstrated that it had no relation to spina bifida. He believed that hygroma was a new formation independent of the development of the fetus. Bruch,[2] opposing the idea of Wernher, felt that there was no evidence of pathologic, neoplastic tissue in hygroma cysticum. He thought that serous effusion or extravasation into the subcutaneous tissues constituted the primary and important factor. Rokitansky [3] believed that this type of cystic tumor resulted from a tissue-limiting process around an edema or serous exudate occurring in the fetus. The limiting walls were formed from the thickened preexisting connective tissue which surrounded the fluid. The lining of the walls subsequently became smooth, whereupon a secretory balance occurred between the walls and the fluid. Gurlt [4] reviewed all the known cases up to his time. He accepted the view of Rokitansky and referred to the condition as "hydrops universalis," although he could not explain the characteristic hydropic secretion in various organs or the occurrence of the tumor in four favorite localities. As early as 1861, Storch [5] gave a good description of the clinical course of cystic hygroma. Luschka [6] considered the possible origin of hygroma from the ganglion intercaroticum because of the tendency to cystic degeneration of this organ.

Thus the view of Wernher that hygroma represented a new formation and was unrelated to developmental anomalies of the fetus was opposed for twenty years, until it was championed by Virchow. Thereupon Wernher's view was generally accepted. Virchow [7] discussed the term "hydrocele," which had been used by various authors to designate tumors composed of closed sacs containing a watery fluid. If the sacs

1. Wernher, A.: Die angeborenen Kysten-Hygrome und die ihnen verwandten Geschwülste in anatomischer, diagnostischer und therapeutischer Beziehung, Giessen, G. F. Heyer, Vater, 1843, p. 76.

2. Bruch, C.: Zur Entwicklungsgeschichte der pathologischen Cysten-bildungen, Ztschr. f. rat. Med. **8**:191, 1849.

3. von Rokitansky, C.: Lehrbuch der pathologischen Anatomie, ed. 3, Vienna, W. Braumüller, 1855, vol. 1, p. 230.

4. Gurlt, E.: Ueber die Cystengeschwülste des Halses, Berlin, T. C. F. Enslin, 1855.

5. Storch, O.: Ueber das angeborene Hygrom des Halses, J. f. Kinderkr. **37**: 68, 1861.

6. Luschka, H.: Ueber die drüsenartige Natur des sogenannten Ganglion intercaroticum, Arch. f. Anat. u. Physiol. **4**:405, 1862.

7. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863, p. 170.

of the tumor were small, the term hygroma was applied; if they were large, hydrocele was used. Thus the terms hydrocele colli and hydrocele capitis arose in the classification of tumors which were in many instances probably true hygromas. Virchow objected to these terms, because he doubted that the fluid in these tumors occurred in preexisting true anatomic sacs. He considered "hydrocele colli" an obscure formation in which the sacs were newly formed and contained an encapsulated fluid which was probably a transudate.

Arnold [8] reported 2 cases of hygroma colli cysticum and convinced himself that the growths did not arise from the intercarotid ganglion since the cystic cavities were lined with endothelium. In his second case, he described atrophic muscle fibers coursing through the cystic tumors. His conception of the growth of the tumors was that the cellular elements of true connective tissue disintegrate, forming round cystic spaces in which fluid accumulates secondarily.

Koester [9] made one of the first important contributions to the subject. By means of silver solutions, he demonstrated an endothelial lining in the cysts of a cervical hygroma. He concluded that the cystic cavities of hygroma arise by a widening of preeixsting lymph vessels and that this accounts for the penetration of the tumors into surrounding organs and tissues. He designated the hygromatous tumors as "lymphangiectasia congenita." Borst [10] studied lymphangioma located within a lipoma and offered evidence of the formation of new lymph capillaries from the intercellular canalization of buds which sprouted from the endothelial lining of the dilated lymph vessels and penetrated the adjacent connective tissue. However, he did not observe this phenomenon in hygroma and therefore was unable to say whether hygroma develops merely from preexisting lymph spaces or by the actual growth and propagation of newly formed lymphatics. Accordingly, the etiology and manner of growth of hygroma remained obscure.

Langemak [11] discussed the possible development of hygroma from subcutaneous bursae not connected with the joints. Opokin [12] felt that the new cysts of the growing hygroma arise from developmental changes

8. Arnold, J.: Zwei Fälle von Hygroma colli cysticum congenitum und deren fragliche Beziehung zu dem Ganglion intercaroticum, Virchows Arch. f. path. Anat. **33**:209, 1865.

9. Koester, K.: Ueber Hygroma cysticum colli congenitum, Verhandl. d. phys.-med. Gesellsch. in Würzb. **3**:44, 1872.

10. Borst, M.: Die Lehre von den Geschwülsten, Wiesbaden, J. F. Bergmann, 1902, vol. 1, pp. 191-204.

11. Langemak, O.: Die Entstehung der Hygrome, Arch. f. klin. Chir. **70**:466, 1903.

12. Opokin, A.: Zur Lehre über die Patho- und Histogenese des Lymphangioms (Ein Fall von kavernösem Lymphangiom der Halsgegend beim Erwachsenen.), Frankfurt. Ztschr. f. Path. **9**:143, 1911.

in certain large polygonal or pear-shaped cells which are found in the stroma. In his opinion cysts are formed by the degeneration and liquefaction of the central cells of a mass, with the formation of cavities which later become lined with endothelial cells. Four drawings were shown which were supposed to illustrate this process. Dowd [13] reported 4 cases of hygroma which he had observed personally and appended a table, prepared by Farr, in which the cases of hygroma reported in the literature up to 1913 were summarized. There were 91 instances of hygroma occurring in the neck and 35 of hygroma located principally in the axilla. McClure [14] interpreted Dowd's specimens in the light of his own comparative anatomic studies on the lymphaticovenous communications in adult mammals. He suggested that hygromas probably arise from sequestrations of lymphatic tissue derived from the primitive jugular sacs. Dowd accepted this view and believed that these lymphatic rests possess an independent power of irregular growth.

Ribbert [15] agreed with Borst as to the manner of growth of lymphangioma, but he believed that the peculiar power of the hygromatous tumor to penetrate muscles, glands, nerves and other tissues differentiates it from lymphangioma. He felt that this power of penetration was understandable only on the basis that the endothelium sends out shoots which later become canalized and thus give rise to cysts. He admitted that the growth of hygroma was probably similar to that of lymphangiomas, but he could not prove his point by microscopic studies. Interesting individual cases of hygroma have been reported by Mathews,[16] Lyle [17] and Downes.[18] Hadley,[19] who reported a case of retroperitoneal cystic tumor, drew attention to the similarity of the histologic structure of the wall in this tumor to that in hygroma colli cysticum. From this he concluded that certain of the retroperitoneal tumors likewise originate from the primitive lymph sacs.

Thompson and Keiller [20] in 1923 reported 2 cases of hygroma, a tumor which they regarded as the cystic form of cavernous lymph-

13. Dowd, C. N.: Hygroma Cysticum Colli: Its Structure and Etiology, Ann. Surg. **58**:112, 1913.

14. McClure, C. F. W., and Silvester, C. F.: A Comparative Study of the Lymphatico-Venous Communications in Adult Mammals, Anat. Rec. **3**:534, 1909.

15. Ribbert, H.: Geschwulstlehre für Aerzte und Studierende, Bonn, F. Cohen, 1914, pp. 226-231.

16. Mathews, F. S.: Hygroma of Neck, Ann. Surg. **59**:753, 1914.

17. Lyle, H. H. M.: Cystic Hygroma of Neck: Excision, Ann. Surg. **60**:398, 1914.

18. Downes, W. A.: Hygroma of Axilla and Neck, Ann. Surg. **59**:753, 1914.

19. Hadley, H. N.: The Origin of Retroperitoneal Cystic Tumors, Surg., Gynec. & Obst. **22**:174, 1916.

20. Thompson, J. E., and Keiller, V. H.: Lymphangioma of the Neck, Ann. Surg. **77**:385, 1923.

angioma. They agreed with Dowd as to the probable origin of hygroma from lymphatic rests derived from the jugular sacs. They observed microscopically that the walls were made up of inactive lymphatics, and the lining endothelium of the cyst itself contained few cells in the process of division. Therefore, they concluded that the extension of hygroma into the axilla and the mediastinum is not due to an invasive power on the part of the endothelium. According to this view it actually originates in anlages occupying these regions but lies quiescent until cyst formation causes it to appear as a visible swelling. Vaughn [21] reported a case of cystic hygroma of the neck and in considering the etiology agreed with Thompson and Keiller as to the origin of cystic hygroma. These views were accepted likewise by MacGuire,[22] who reported the history and the pathologic observations in a case of hygroma and referred to 7 others. He advised against radical operative procedure when roentgenograms show mediastinal extension of the tumor.

Dowd and Ribbert suggested that hygroma colli cysticum is derived from lymphatic rests which are remnants of the primitive jugular sacs and which possess an independent power of irregular growth and penetration. This view has in recent years been rather generally accepted, although support for it has heretofore not been offered. I believe that the pathologic studies subsequently to be reported provide histologic evidence of the specific conditions characterizing the origin and development of cystic hygroma. By presenting this evidence I hope to clarify the obscure nature of this tumor.

ANALYSIS OF CASES OF HYGROMA

Etiology.—According to the most plausible theory, hygroma arises from sequestrations of lymphatic tissue, derived in the case of cervical hygroma from the jugular sac, which retain their independent power of irregular growth. Comparative anatomic studies of the development of the lymphatic system were made by McClure and Silvester.[14] In figure 1 is shown the relation of the left jugular lymph sac of an 11 mm. cat embryo to the internal jugular and subclavian veins before the jugular and subclavian approaches have joined with the venous system. Figure 2 illustrates the structure of the lymphatics and their ultimate communications with the veins in the pig-tailed macaque.

In order to elucidate this theory, it may be well to review briefly the knowledge of the early development of the lymphatic system. Sabin [23]

21. Vaughn, A. M.: Cystic Hygroma of the Neck: Report of Case and Review of Literature, Am. J. Dis. Child. **48**:149 (July) 1934.

22. MacGuire, D. P.: Cystic Hygroma of the Neck, Arch. Surg. **31**:301 (Aug.) 1935.

23. Sabin, F., in Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Co., 1912, vol. 2, pp. 709-716.

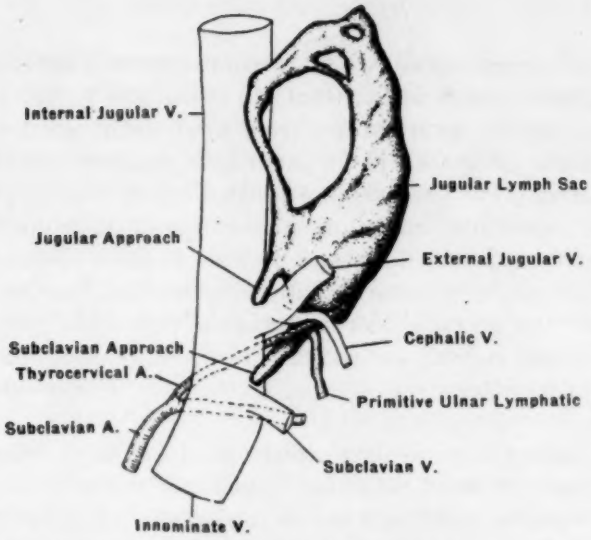

Fig. 1.—A reconstruction of the left jugular lymph sac of an 11 mm. cat embryo (Felis domestica), showing the jugular and subclavian approaches through which the two typical adult communications are established between the lymphatics and the veins. Reproduced from McClure, C. F. W., and Silvester, C. F.: A Comparative Study of the Lymphatico-Venous Communications in Adult Mammals, *Anat. Rec.* **3**:535, 1909.

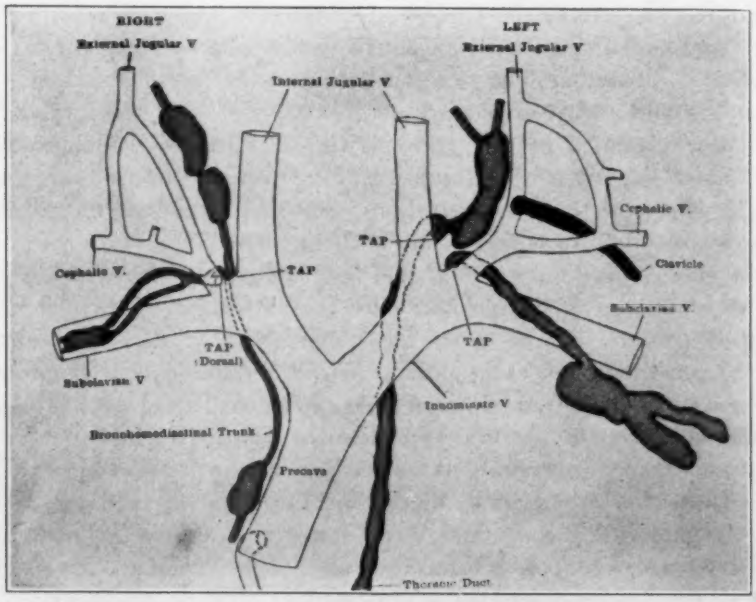

Fig. 2.—The structure of the lymphatics and their communications with the veins in the pig-tailed macaque (Macacus nemestrinus, Linn). (Reproduced from McClure, C. F. W., and Silvester, C. F.: A Comparative Study of the Lymphatico-Venous Communications in Adult Mammals, *Anat. Rec.* **3**:551, 1909).

presented a new conception of the general structure and development of the lymphatic system in the fetus. In the primary stage of development a capillary plexus is formed from the jugular vein on each side. In certain areas along this vein, a part of the capillary plexus is cut off from the parent vein. This group of isolated spaces lined by endothelium remains for a short time, constituting the anlage of the lymphatic system. These isolated capillaries dilate and coalesce to form symmetrical lined sacs. In this manner the two primitive jugular sacs, one on each side, are formed. The thoracic duct connects the pelvic and retroperitoneal sacs with the left jugular sac and then forms an opening into the veins at the jugular valve. On the right there is a somewhat similar development.

The secondary stage of development involves the peripheral growth of the lymphatic vessels. Sabin has shown that this is accomplished by endothelial sprouts, which are derived from the lining of the jugular sacs and which penetrate the surrounding tissue and radiate outward over the body. In addition, there is the element of secretion from the endothelium of the newly formed lymphatics. This is the normal course of development of the lymphatic system. Through some anomaly of growth, fibrosis or other accident the primitive jugular sac (fig. 1) or portions of it may fail to establish a communication with the venous system. The lymphatic tissue thus sequestrated may retain the power of growth inherent in the process of endothelial sprouting and penetration characteristic of the development of the normal lymphatic system (Sabin [28]). These are the two factors necessary for an explanation of the origin and growth of cervical hygromas.

The explanation of the origin of the sequestrated lymphatic tissue still lies in the realm of assumption. However, the origin and growth of hygroma from these sequestrations, which have retained the power of growth just described, need hardly be assumed any longer in view of the studies here reported. It will be histologically demonstrated that hygromatous cysts arise primarily by the formation of fibrillar membranous sprouts derived from the lining walls of the cystic spaces. By the penetration into surrounding tissues and subsequent canalization of these sprouts, cysts are formed and propagate themselves in a manner somewhat analogous to the development of the early lymphatic system.

Predisposing or exciting causes are not known. Wassermann and Kahn tests were done in a number of instances on both the patient and the patient's parents and were uniformly negative. Tuberculous ancestry was present in 1 instance (case 4), and trauma seemed to be an activating cause in another case (case 1).

Symptomatology.—In the majority of cases of less advanced involvement the symptoms of hygroma were negligible except for worry

over the disfigurement or the nature of the tumor itself. The definite symptoms present in the 6 cases in which the process was more advanced were due to mechanical interference with certain functions as a result of the location, size and weight of the tumor. They resulted from pressure on an important structure, such as the trachea, pharynx, floor of the mouth (case 4) or mediastinum (case 9), or on an important nerve trunk, such as the cervical or brachial plexus (case 7). (As the tumors are soft and fluctuant, they are readily molded about the denser structures and may thus attain a large size before causing symptoms of mechanical pressure.) Three patients (cases 3, 5 and 9; figs. 33 and 36) complained of mechanical interference with the movements of the head and neck. In 1 instance (case 2; fig. 13) the tumor prevented free action of the right arm.

Serious symptoms occurred where there was direct pressure on important structures. Respiratory embarrassment (case 9) was due to mediastinal obstruction of the trachea (fig. 47), which was shown by roentgen examination to be displaced far to the left. As a result the child was a "blue baby" at birth. Interference with deglutition due to encroachment on the pharynx also was present in this case. Pain, paresthesia and weakness or loss of function of an extremity were occasionally noted. Pain radiating to the right ear and right side of the neck and weakness and paresthesia of the right arm were referable to the hygromatous mass in 1 case. It was discovered at operation that the tumor lay directly on the cervical and brachial plexuses (case 7). It is interesting to note that in this case stiffness of the neck and weakness of the arm had been noticed before the patient became aware of the tumor. Incidentally, there was in this case a perfect trigeminal cardiac rhythm, which was observed to be regular several months later as noted at the follow-up examination.

Symptoms and complications due to secondary infection may account for prolonged drainage after operative treatment. Infection has in a number of reported cases accounted for a fatal outcome. (This is readily understood when one considers the multilocular cystic nature of the tumor and its common location in the neck, where it is subject to secondary infection from tonsils and pharynx.) In a patient at the Long Island College Hospital (case 9), there was a severe secondary acute adenitis and infection of the hygromatous tumor arising from a streptococcic infection of the throat. The streptococcus was recovered in culture from the tumor. Drainage from the operative wound was prolonged and the healing slow. Infection of the wound (case 10) followed immediately on secondary operation for recurrence, at which time an acute infection of the upper part of the respiratory tract developed.

Complications may occur also as a result of infection produced by operative incision, followed by prolonged drainage of infected secre-

tion, as in case 4. There was rapid growth of the tumor, with associated glandular enlargements in the right cervical region due to infection with the streptococcus (case 9). In some ways it resembled the development of a malignant growth. There were no symptoms of general systemic character in any of the 12 cases except that in case 2 there was some mental dulness, which might have been due to markedly hypertrophic tonsils and adenoids. Very young children with hygroma, however, often are below par and suffer from anemia. In general, there were few direct or secondary complications, as indicated in 8 of the 12 cases. The tumors were rarely painful or tender. A recurrent tumor may cause symptoms notwithstanding that the primary growth may not have produced any. In case 10, for example, the floor of the mouth became involved after the removal of a hygroma in the upper anterior cervical triangle.

Gross Pathologic Picture.—The characteristic appearance of the tumor which has been surgically removed is that of a multilobular, multilocular cystic mass, in which the individual cysts vary from the size of a pinhead to that of a lemon. The walls of the younger cysts are extremely thin, delicate, friable and practically transparent; the walls of the older cysts are often thick and fibrotic (fig. 7). There is frequently generalized fibrosis in the older portions of the tumor, and consequently fragments of adjacent muscles, fascia, nerves and blood vessels are adherent to the excised mass.

In certain areas the mass is often spongy, giving the appearance of the ordinary rubber bath-sponge (figs. 42 and 45); in other areas there are large whitish zones of fibrosis. The cysts themselves are usually soft and fluctuant but rarely tense. The fluid within the cysts is serous, watery, clear or straw colored and occasionally turbid or blood stained. Not uncommonly the mass is intimately associated with groups of enlarged lymph glands, which are hyperplastic (figs. 11 and 12), at times edematous and occasionally fibrotic. These glands are encountered in the walls of the tumor and are thus doubtless directly involved in the pathologic process. The cystic spaces within the tumor are found to be lined by a thin, pearly white, glistening almost transparent membrane which resembles peritoneum or pleura. The cavities, together with their many recesses, septums and trabeculae, are lined in a similar manner. The trabeculae are often seen as isolated cords traversing the cystic cavities (fig. 14 *A* and *B*). Any remnants of muscle which are attached to the outer margins of the tumor often show separation and atrophy of the individual bundles, produced by the interposition of hygromatous tissue and cysts (figs. 14 *A*, VI and VII, 18 *A*, 30 and 31).

Microscopic Pathologic Picture.—Sections varying in thickness from 6 to 8 microns were cut from blocks of tumor tissue fixed in solution

of formaldehyde and Zenker's fluid. These sections were stained, for the most part, with hematoxylin and eosin. Mallory's aniline blue collagen stain was employed for the demonstration of collagen fibrillae; Van Gieson's stain, for connective tissues; Verhoeff's method, for elastic fibers, and osmic acid, for evidences of fatty degeneration.

Endothelial Lining: Flat sections stripped from the lining of a large fresh cyst were spread on glass slides and treated with a 3 per cent solution of silver nitrate, which was reduced by sunlight. The reduced silver salt was precipitated in the intercellular cement substance and thus outlined in black the margins of the lining cells. This process revealed a single layer of elongated, hexagonal cells characteristic of the endothelial lining of the blood and lymph vessels (fig. 15). The lining cells of the hygromatous cysts were seen to be of true endothelial nature and to differ from the characteristic mesothelial lining of cavities such as joint cavities or bursae.

Cyst Walls: The older cysts, like the smaller ones, are lined by endothelium (figs. 7 and 20). Their walls are thick, fibrotic and hyaline, at times almost avascular (fig. 7), whereas the thin, delicate walls of the younger cysts may consist of little more than two layers of endothelial cells separated by a few intervening connective tissue fibers and occasional small blood capillaries (fig. 16). Below the endothelial layer, there is often a zone of loose, extremely fine, lacelike reticulum composed of areolar connective tissue which resembles very fine adipose tissue (fig. 41). This characteristic reticulum acts as a ground substance for all the variable microscopic pictures that one sees in the different types of hygromatous stroma. Its meshes are frequently filled with lymphocytes, lymphoblasts, epithelioid cells and newly formed capillaries (fig. 39). In the stroma between the cysts proper and in the periphery of the tumor, one may see lymph sinuses of all sizes and considerable numbers of large and small arteries and veins (fig. 40). The deep portions of the thick peripheral walls often contain layers of dense hyaline connective tissue together with a delicate reticular adipose tissue.

Lymphoid Tissue: In many areas in the thin and apparently younger cystic walls characteristic dense aggregations of lymphoid cells are observed (fig. 4). These aggregations vary in size from groups of a few cells to large accumulations containing true follicles with germinating centers, which resemble those in lymph glands (fig. 5). These larger aggregations of lymphoid cells are richly supplied with small blood vessels and contain a considerable number of plasma cells. Lymphoblasts and plasma cells are seen predominantly in the newly formed germinating centers of the lymph follicles. Transitions from the lymphoblastic cell to the true lymphoid cell are seen in the periphery of the germinating centers. It is to the lymphoblasts, it seems, that

Opokin [12] attributed the potentiality of forming new cysts and of metamorphosis into true endothelium. No evidence of such changes was observed in these studies.

It appears from the large number of transitional cells that hygromatous tissue itself is capable of producing an abundance of lymphoid tissue, germinating lymph follicles and possibly even lymph glands. Thus accumulations of lymphoid cells, both in the form of follicles and of large, dense zones (figs. 38 and 39), are produced from the endothelium in the cyst wall and do not represent infiltrations.

Lymph Glands: Groups of enlarged hyperplastic lymph glands are generally intimately associated with the hygromatous tumors. An illustrative example of such a gland is shown in figures 11 and 12. The lymph follicles are increased in number, and the germinating centers contain numerous lymphoblastic cells of various sizes and shapes, together with epithelioid cells and those of endothelial type. There is a striking frequency of karyokinetic figures in the germinating centers. The hilus of the hyperplastic lymph gland contains many large lymph sinuses, which are commonly entirely filled with lymphoblastic, lymphoid and epithelioid cells. Large blood spaces also are common.

Trabeculae: Densely fibrotic isolated and free trabeculae (fig. 14 *A*, III) are occasionally seen coursing through the cystic cavities of hygroma. Cross sections of such trabeculae (fig. 8) show that they are lined by endothelium similar to that of the cystic cavity. They reveal, moreover, that the trabeculae represent the persistence of arteries, which remain after the cyst walls in which they formerly ran have atrophied and disappeared. Thus the centers of the trabeculae show hyalinization of organized clots following thrombosis (fig. 8), and the peripheral zones show concentric hyalinization of the walls of the old artery. (The fibrosed vessels thus remain as isolated cords or trabeculae traversing cystic cavities in a fashion similar to the coursing of vessels through an old tuberculous or other abscess cavity.)

Stroma at the Growing Margin of Hygroma: The manner in which hygromatous cysts grow and propagate and their potentiality of destroying adjacent anatomic structures is made clear by a study of sections taken from the growing margin of a hygromatous tumor. In order to obtain and preserve conditions as much like those in living tissue as possible, the fresh tumor should be distended with an appropriate fixative, such as solution of formaldehyde, before its final immersion in the fixing fluid. If the cysts and their walls are allowed to collapse after the loss of their fluid, the microscopic characteristics peculiar to hygroma are largely destroyed, and histologic sections therefore fail to reveal them.

The histologic characteristics of the growing margin of a hygromatous tumor properly distended and fixed are well illustrated in the zone where the hygroma meets a normal anatomic tissue, such as a mass of

muscle (figs. 14 *A* and 17). The fine areolar fibrillar stroma in the walls of the marginal cysts penetrates and destroys large areas of adjoining muscle (fig. 18). The penetrating stroma separates and isolates the muscle fibers, which finally undergo pressure atrophy and degeneration. At times bands of muscle fibers are found running along in the partitions between adjoining cysts which have penetrated the main muscle. At area I, figure 14 *A*, such a band of muscle fibers was compressed in the wall between two adjoining cysts. The individual muscle fibers showed microscopically atrophic, hydropic and fatty degeneration resulting from the pressure exerted by the cysts. (Attention is drawn to the photograph of a gross specimen, figure 14 *A*, in which the penetration of marginal cysts has separated the deltoid muscle into a number of subdivisions, which are finally lost in the walls of the cysts.)

Endothelial Sprouts: On detailed study of the cyst walls and stroma at the growing margin of a hygroma, further interesting observations are made on the manner in which this tumor penetrates adjoining normal tissues. In figure 17 is illustrated the growing edge of a hygroma, which comprises a marginal cyst, the stroma of its walls and the adjoining deltoid muscle. The fine delicate membranes which appear in the microscopic section as bands or cords are composed of endothelial and connective tissue fibrillae. They radiate from the lining wall of the cyst and in serpentine fashion penetrate the clefts of the adjacent tissue, in this case a mass of muscle. At a distance of 2 to possibly 3 mm. or more from the endothelial lining of the cyst, they are no longer recognizable. They terminate in several fibrillae, which are lost in the tissues.

These radial sprouts in turn send off lateral branches into the tissue clefts. In the high power magnification they are seen to be composed of extremely delicate fibrillae in parallel arrangement and well supplied with thin, elongated, flattened or spindle-shaped nuclei of endothelial type (figs. 9 and 10). Between these fibrillae are frequently seen lymphoid cells and, at varying intervals along the sprouts, droplets of foamlike, faintly blue-staining secretion, doubtless the earliest produced by the endothelial fibrillae. The droplets are identical in appearance with the bluish, frothlike, coagulated contents seen in the larger and older definitely formed cystic spaces. As a result of continued secretion the droplets enlarge and are then enabled to spread apart and finally canalize the fibrillae. These thereupon form the limiting endothelial walls of the newly formed lymph capillaries and minute cysts.

This process is well illustrated in figure 17, circle *D*, and figures 19 and 20, which show a cystic cleft formed by the accumulation of lymph within the fibrillae of a characteristic endothelial sprout in a cleft of muscle. The endothelial lining of this newly formed cyst is clearly indicated in figure 20 and is perceived to be continuous with the fibrillae

of the sprout in which the cyst is enclosed. New cysts are brought into being by this characteristic process of secretion within and subsequent canalization of the fibrillae composing a sprout. These minute young cysts are commonly in intimate association with the walls of the larger cysts (figs. 10 and 17).

Circumscription and Isolation of Anatomic Structures: As these fibrillar membranous sprouts penetrate adjacent tissues they characteristically circumscribe and isolate anatomic structures that lie in their paths, such as muscle fibers, nerves and blood vessels. Thereupon a cyst may form around such a structure. This formation is manifested in figures 9 and 10, in which the fibrillae are seen to enclose a nerve fiber at *N*. This gives rise to a perineural lymph space and then continues onward to form a small cyst. In this process of circumscription the nerve, muscle fiber or other structure receives an endothelial covering and is subsequently sequestrated in the lymphatic or cystic fluid secreted by the fibrillae surrounding it.

Attention is directed to figures 9 and 10, in which a bundle of muscle fibers covered with endothelium is seen lying free and sequestrated in a small cyst. The cyst in turn is lined by a layer of thin, flattened endothelial cells and subendothelial connective tissue and filled with a bluish (hematoxylin), foamlike coagulated lymph. The sequestrated muscle fibers show vacuolar hydropic degeneration and fragmentation. The fibrillar stroma immediately surrounding the cyst is invading and destroying an area of muscle fibers, most of which show evidences of degeneration, fragmentation and approaching solution. Thus anatomic structures are circumscribed by the endothelial sprouts, and tissues are sequestrated within the cysts formed by subsequent secretion between the fibrillae of the sprouts. This process is observed in many sections from the growing edge of hygroma.

Death and Solution of Tissue Included in the Cysts: A study of the sections reveals the ultimate fate of the normal tissues which have been engulfed in the cysts. Deep in masses of muscle, the cysts enclose fragments of muscle fibers (figs. 25 and 26). These fibers engulfed within the cysts show early evidences of atrophy and fatty degeneration, losing much of their affinity for stains. The striations, still apparent in some of the fibers cut longitudinally, indicate that their sequestration is a fairly recent event and that the cyst is young. As the cysts enlarge, pressure atrophy is noted in the tissues surrounding them.

In the cysts in which the process of sequestration is an older one, degeneration of the included tissue is more advanced. The muscle fibers in such an instance show extensive hydropic degeneration, disintegration and almost complete solution. Here and there faint striations are still apparent (figs. 23 and 24). Finally only isolated fragments of

muscle or other included tissue are seen, together with remains of degenerated cells, conglomerate nuclei and cellular débris (figs. 21 and 22). Cellular débris and groups of cells of lymphocytic, endothelial, epithelioid and large mononuclear types are often found in the fluid of the older cysts, particularly after centrifugation of the fluid. Eventually complete liquefaction of the sequestrated tissue fragments occurs. Nerve fibers may be destroyed in a manner similar to that described for muscle fibers (figs. 21 and 22). A nerve fiber the elements of which have been separated by endothelial ingrowth and circumscription is shown within a cyst.

Destruction of Muscle Fibers by Hygroma: The manner in which the infiltrative edge of a growing hygroma injures and finally destroys individual muscle fibers is seen in figures 23 to 29. These illustrations present a study of sections from the zone of contact (area VI, fig. 14 *A*) between the hygroma and a mass of adjacent muscle. The stroma of the tumor sends out fine fibrillae, which are well supplied with nuclei of endothelial type and which are usually derived from the walls of preformed cysts or lymph spaces. These fibrillae penetrate and infiltrate between the fibers and frequently surround and isolate an individual fiber. Thus in the muscle in close proximity to the hygroma one recognizes the damaging effect of this growth. The caliber of the muscle fibers varies greatly because of atrophy and degeneration of the individual units (fig. 27), which show variations in their affinity for stains.

Another interesting phenomenon observed is the occurrence of numerous transverse fractures of the weakened fibers, due doubtless to their inability to withstand the strain of the contraction of the muscle. (The transverse fractures of the muscle fibers here described were observed in a patient recently operated on, whose sternohyoid muscle showed infection with Trichinella spiralis.) At the margin of the muscle immediately involved by the growing stroma, the fibers show further atrophy and fatty degeneration, tapering off and finally disappearing in the direction of the tumor (fig. 28).

The penetrating endothelial fibrillae may surround and isolate an individual fiber in a small bundle and involve the remaining fibers of the bundle less extensively. Thus one sees segments of fractured muscle fiber enclosed within fibers which show only beginning atrophy and degeneration. The segments of broken fiber are swollen because of hydropic degeneration and devoid of their striations, whereas the surrounding fibers present a relatively more normal appearance (fig. 29). The endothelial fibrillae enclosing the segments of fractured fiber then begin to secrete and to form an early minute cyst. The endothelial lining of this newly formed cyst is continuous with the fibrillae enclosing the fragments of muscle which it is destined eventually to engulf. Once

engulfed, the fragments liquefy and disappear; thus a muscle fiber has been destroyed. This process is then repeated indefinitely.

Connective Tissue: Hygromatous stroma, composed of endothelial and connective tissue sprouts derived from the walls of the cysts, has been illustrated (figs. 17, 21 and 30). Further histologic investigation reveals that this infiltrating stroma is composed of bundles of fibers, arranged in parallel strands, and a reticular network. These fibrillar membranes on differentiation with Mallory's aniline blue method are seen to be comprised of blue-staining collagen fibrillae and deep orange or reddish fibers. They contain also a large number of fine elastic fibrillae demonstrable after the method of Verhoeff. The elastic tissue occurs in relative abundance in the stroma of the cyst walls. Van Gieson's stain for connective tissue imparts to the infiltrating fibrillar membranes a rich red stain, thus sharply differentiating them from the muscle (fig. 30).

Fatty Degeneration of Muscle and Formation of Adipose Tissue: As a result of the infiltration of the muscle with hygromatous stroma and the circumscription of individual muscle fibers, the latter undergo atrophy and fatty degeneration (fig. 31). Fat droplets, stainable by osmic acid and sudan III, accumulate within the muscle fibers before the contour and striations of these fibers indicate their loss of identity. These fat droplets increase in size and number and coalesce to form large globules of fat. The peripheral fibrillae of an individual fiber are often seen still enclosing the fat globules. Finally all the fibrillae disappear, and only the outlines of a fiber, replaced by fat globules, remain (fig. 32).

This replacement of muscle fibers by true adipose tissue is a characteristic process at this stage. The former muscle fibers, transformed into fat, coalesce to form large areas of adipose tissue (fig. 32), frequently seen in the walls of large cysts and adjacent regions. This adipose tissue is therefore the end result of the destructive action of hygroma on normal tissues.

Nature of the Cystic Fluid.—Unless infection (case 4) or hemorrhage (case 2) has occurred, the fluid characteristic of hygromatous cysts is thin, watery and clear or straw colored. It is practically free of albumin and globulin and does not coagulate on cooling. Storch [5] mentioned that in 2 cases which antedated his own observations there were respectively 4 per cent and 11 per cent of protein in the fluid. The method of determining the amount of protein was not given. Cholesterol crystals in large numbers are often seen floating on the surface of the fluid, particularly in cases in which hemorrhage with hemolysis has occurred. In the fluid from a typical, uncomplicated tumor, the sediment thrown down by centrifugation showed small numbers of lymphocytes,

mononuclear cells, large phagocytes, occasional polymorphonuclear cells and cholesterol crystals (case 1).

The fluid in case 2 was turbid and light brownish and did not coagulate. It contained large numbers of cholesterol crystals, achromic degenerated red cells and phagocytes in which hemosiderin crystals were seen. This specimen gave a moderately positive reaction for albumin and globulin. These peculiarities were doubtless the result of hemorrhage. In an additional case the fluid was jellylike and pale yellow, presumably owing to infection (case 4). Similarly, the fluid was thick in case 9, in which the hygroma was secondarily infected. It coagulated on standing, and streptococci were found in the culture.

Growth of the Tumor.—In the majority of cases, the tumor is first noticed at birth or in the early years of childhood. It may, however, make its first appearance in adult life. In 2 patients (cases 7 and 12), the mass was first noticed at the ages of 38 and 34 respectively. When first discovered, the tumors varied from the size of a hazelnut to that of a golf ball. The mass may enlarge rapidly and reach a considerable size in from a few weeks to several months (case 3). On the other hand, it may grow slowly over a period of years, as in case 12, in which the tumor reached the size of a hen's egg in six years. Slow, progressive growth is the rule in the majority of cases, although there may be prolonged periods of relative quiescence. Fluctuations in size are frequent and often marked. Complete disappearance of the tumor for a considerable period has been noted. In case 5 there was a history of several regressions of the tumor during a period of twenty years, after which time it attained the size of an orange. At the time of operation the tumors varied from the size of a walnut to that of a child's head. In the cases of the 7 infants there was a history of gradual enlargement of the tumor since birth.

Incidence.—Hygroma occurs somewhat more often in females than in males. In the 12 cases reported here, 7 girls and women and 5 boys were involved. The tumor was first noticed at birth in 4 cases, and in 1 other, within the first year. In the remaining 7 cases the tumor occurred at varying ages up to 38. The majority of the patients were children under 12 years of age. The duration of the tumor from the time it was first noticed to the time of operation varied from six weeks to twenty years. In most instances the interval was from one to three years. There were 10 white and 2 Negro patients.

Location.—It is interesting to note the location of the tumors. The mass was on the left side in only 3 cases, in which it involved the anterior and posterior triangles, the left submandibular region and floor of the mouth and the left submaxillary and anterior cervical triangles respec-

tively. In the remaining 9 cases the tumor occurred on the right side. The areas involved were the right anterior cervical triangle and mediastinum once, the right cervical anterior triangle alone once, the right submandibular and posterior triangle once, the posterior triangle twice, the anterior midneck once, the right shoulder and arm once and the axilla twice. There was no case of bilateral involvement.

Diagnosis.—Errors in the diagnosis of hygroma before operation are frequent, and at times a correct diagnosis is well-nigh impossible. These presumptive diagnoses were made before hospitalization: hematoma, angioma, tuberculous adenitis, simple cyst, lipoma, bronchial cyst, goiter and benign lymphatic tumor. After the usual period of study in the hospital, the preoperative diagnosis was correct in 7 of the 12 cases. In the remaining 5, the tumor was thought to be a cyst originating in the lymphatic glands or the branchial cleft: a simple cyst in 1, a lipomatous tumor in 1 and a growth of undesignated type in the remaining 3. The diagnoses of lymphoblastoma, Hodgkin's disease and acute cervical adenitis with abscess had been suggested in the case of hygroma secondarily infected.

A positive clinical diagnosis can usually be made from the history and the results of physical examination. There is commonly a history of a soft, fluctuant, multilocular mass appearing at birth or in early childhood in the lateral cervical region or in the axilla and slowly increasing in size. As a rule the tumor is not tender or compressible. The overlying skin is not adherent, and its thinness may give the mass a bluish, translucent appearance. Accordingly, the tumor transilluminates well when a bright light is applied. Fluctuations in size are common, and there may be a history of temporary complete disappearance with subsequent reappearance. There may have been periods of infection during which the mass was inflamed, tender, tense and associated with toxemia. The tumors are diffuse in appearance, poorly circumscribed and inclined to involve neighboring structures in their growth. In various areas of the soft mass, irregular firm nodules, which may be trabeculae, areas of fibrosis or groups of lymph glands, are often palpable. The regional lymph glands are, as a rule, not enlarged.

Differential Diagnosis.—Since the preoperative diagnosis of hygroma appears difficult, the two principal conditions with which it may be confused should be mentioned, namely, cyst originating in the branchial cleft and lipoma. Cysts of the branchial cleft are likely to be single, rounded or oval, unilocular and smaller than hygroma. They are rather tense, firm and well circumscribed; often deep-seated, they occur principally in the anterior triangle. There is no associated atrophy of the overlying fat and skin. Furthermore, on gross and microscopic exami-

nation the branchial cyst is seen to have a thick capsule and a lining of stratified squamous epithelium or columnar cells, which may be ciliated. The content of the branchial cyst is either a thick, heavy, tenacious mucus, or a grumous, fatty accumulation of cellular débris. The lipomatous tumor is less well defined because of its deep-seated location and is usually not as definitely fluctuant. Fine lobulations may possibly be palpated in lipomas; they do not transmit light; the overlying fat and skin are not atrophic, and they grow less rapidly.

The differential diagnosis from tuberculous adenitis, cervical abscess and goiter need hardly be considered. Hygroma is readily differentiated from malignant tumors because it lacks the definite firmness of the latter and the glandular enlargements associated with them. A cyst of the thyroglossal duct is commonly found in the anterior median line of the neck and is attached to the hyoid bone by a cord which causes it to rise with the act of swallowing. The dermoid cyst is usually recognized by its doughy consistency, while the simple angiomatous tumor is usually compressible.

Clinical Observations.—The general physical examination revealed little or nothing abnormal except such symptoms and conditions as were referable to the tumor itself. There were encroachment on the pharynx, displacement of the trachea, distortion of the jaw and face, muscular weakness, loss of function and neurologic changes due to pressure on individual nerves and nerve trunks. However, in very young infants, the general condition was often noticeably below par; there was apparent anemia, and the skin had a pale and somewhat waxy appearance (case 3).

The erythrocyte count was under 4,000,000 in 3 instances (cases 1, 4 and 9) and below 5,000,000 in the remaining 9 cases. Similarly, the hemoglobin content was low in 4 cases. There was no significant change in the leukocyte count except in the 2 cases in which there was complicating infection (cases 4 and 9), in which it varied between 15,000 and 16,000 cells. There may have been some significance in the occasional increase in the mononuclear count. In 1 patient (case 3) the percentage of mononuclears was 74 per cent, and in several of the others it varied between 31 per cent and 45 per cent.

The temperature and the pulse and respiratory rates remained within normal limits in cases in which there was no complication; the urine was usually normal. The Wassermann and Kahn tests were carried out in about half of the cases and were uniformly negative. No familial history of syphilis or tuberculosis was obtained. In 1 patient (case 9), the hygroma when first observed was tentatively thought to have undergone malignant change; the tumor and its mediastinal extension became progressively larger until high voltage roentgen therapy was instituted.

After this treatment, there was a rapid improvement in the child's condition and a satisfactory diminution was noted in the size of the mass (fig. 47 *A* and *B*).

Clinical Course and Prognosis.—A study of the reported cases and a limited personal experience led Storch [5] to report that, although hygroma was considered a benign tumor, the prognosis was poor. If no treatment was instituted the mass enlarged, sometimes slowly, sometimes rapidly. Death in children resulted from malnutrition. Storch stated further that if a hygroma became infected and if the child survived the infection cure was established. He cited a case of this kind in the experience of Wernher. Figi [24] had never seen a cure follow an infection. According to Boyd, hygroma is seldom met with after puberty, since previous infection results either in death or in spontaneous cure. The mass may involve important structures, such as the mediastinum, with consequent complications. Death, however, is most likely to occur as a result of infection and suppuration following simple incision and the institution of drainage. The tumor may become red and inflamed and be mistaken for an abscess. True suppuration or abscess formation is rare but may occasionally occur. When the hygroma becomes infected, the resulting sepsis is usually severe, as in a case in which there was secondary infection with the streptococcus (case 9). In no instance in this series was there a spontaneous rupture or even threatened rupture of the hygroma. It seems surprising that this accident had not occurred in several cases in which the skin overlying the tumor had become so thin as to be almost transparent.

Treatment.—Since the prognosis with palliative treatment is poor, early and radical surgical resection is the treatment of choice. Various forms of therapy have been tried but have proved ineffectual. Expectant treatment with the hope of spontaneous improvement is a dangerous procedure for two reasons. In the first place, a considerable risk is involved in the possibility of secondary infection in the hygroma following an intercurrent tonsillar or respiratory infection (case 9). Alarming sepsis and toxemia with a resultant fatal outcome may ensue, as in the series of cases reported by Figi,[24] in which a high mortality was due to intercurrent infection. In the second place, as a consequence of prolonged palliative treatment, the hygroma may reach such proportions or may extend so far into inaccessible areas, particularly the mediastinum, as to render surgical removal impossible. The extreme youth of the patients is often considered a contraindication to surgical treatment. Of these patients, 4 of whom were under 3 years of age, only 1, an infant of 6 months, died. This fatality was due to shock caused by

24. Figi, F. A.: Radium in Treatment of Multilocular Lymph Cysts of Neck in Children, Am. J. Roentgenol. **21**:473, 1929.

the prolonged operation necessary for the removal of an extremely large tumor (case 3; fig. 33).

A minor surgical procedure commonly practiced is aspiration. In 2 instances in this series the hygroma was previously aspirated elsewhere. There is no intrinsic harm in aspiration if care is exercised to avoid infection, which may readily occur, particularly when there is leakage from the puncture opening. The diminution in the size of the swelling following aspiration is only temporary, and the reaccumulation of fluid in the tumor is prompt. Aspiration is futile as well as dangerous, except in the small unilocular cysts.

Injection of sclerosing substances in the hope of producing adhesions and subsequent obliteration of the cystic cavities is also ineffectual, since it is impossible to reach all the cysts in the complex multilocular structure characteristic of hygroma. Harrower [25] employed sodium morrhuate as a sclerosing fluid in reducing the swelling in a case of hygroma in a child 1 month of age. The result, he stated, was satisfactory. Another somewhat dangerous and futile treatment is simple incision and drainage. Such incisions have been made in 2 cases in this series, in both of which the infection which followed caused constitutional manifestations and resulted in prolonged drainage (cases 4 and 9). Incision is to be condemned, not only because the infection which will almost certainly occur is difficult to control, but because a subsequent radical operation becomes difficult or impossible.

Because of the unsatisfactory results following the surgical treatment of all multilocular lymph cysts observed prior to 1918 in the Mayo clinic, Figi [24] strongly advocated the nonsurgical treatment of hygroma. In a series of 13 cases which he reported from the same clinic, 12 patients were treated with radium. In only 1 case, in which the hygroma was of limited extent, was excision deemed advisable. One of the cases of Figi's series was reported by New.[26] Aside from this case, Figi's cases are the only instances reported up to 1929 in which radium was employed in the treatment of hygroma.

Figi favored treatment with radium rather than surgical intervention because he felt that the operations were of necessity extensive and the operative risk in young patients was considerable. Excision was not feasible when the mediastinum was involved, and recurrence was rather common even when the tumor was fairly well localized. In children, hygromas treated with radium were reduced in size or disappeared without scarring of the overlying skin. The application of radium did not

25. Harrower, J. G.: Treatment of Cystic Hygroma of the Neck by Sodium Morrhuate, Brit. M. J. **2**:148 (July 22) 1933.

26. New, G. B.: Hygroma Cysticum Treated with Radium, S. Clin. North America **4**:527, 1924.

cause pain, and there were no deaths attributable to the radium, in contradistinction to the reported fatalities after surgical treatment.

Each patient received from one to nine treatments, the average number being four. These figures, however, are only approximate, since some of the patients received further irradiation elsewhere. He reported that 3 of the 12 patients were entirely well, although in 1 of them a very small residual nodule, which might readily be excised, remained. Of the other 9, 2 were much improved and 7 died from an acute infection of the tumor. Four patients of the 7 had infected tumors when they first came under observation; it became necessary to establish drainage in 2 of them, in spite of which 1 promptly died. In 3 patients infection developed during the treatment, and death resulted.

Figi concluded from his experience that radium appeared to be of definite value in the treatment of multilocular lymph cysts in children, that acute infection did not occur more readily after radium treatment for hygroma and that the tumor might disappear or be reduced enough to permit surgical removal. In 2 instances, radium failed to reduce the size of the tumor permanently.

The arguments advanced by Figi for radium treatment in preference to surgical removal of hygroma are largely refuted by the experiences in the excision of hygromas reported in this series. There was only 1 fatality in these 12 cases, although 7 of the patients were infants. The fatal case was that of an infant with an enormous tumor of the right side of the neck, right shoulder and back (fig. 33).

Seven of the 12 patients in Figi's series died of acute infection of the tumor. Four of the 7 patients, to be sure, had an infected tumor when they first came under observation, but in the remaining 3 the infections developed during the course of the treatment. It is difficult to escape the conclusion that irradiation might have increased the severity of the infection in the former and lowered the resistance of the latter. It is well known that lymphatic tissues are peculiarly sensitive to irradiation and that their susceptibility to infection is increased by such treatment. There was only a single prompt recurrence of the tumor in the cases reported in this series. A second excision was followed by a complete cure (case 10).

Furthermore, the cosmetic result after surgical removal of the tumor is far better than that seen after treatment with radium. This is demonstrated in the photograph of the patient reported on by New.[27] Radium treatments had been given for four or five years at intervals of from two months to a year, and several periods of acute infection during the treatment had occurred. The ultimate cosmetic result was poor, for though there was a marked reduction in the size of the tumor, several

27. New, G. B.: Cystic Hygroma of the Neck, S. Clin. North America **11**: 771, 1931.

hard, scarred masses as well as scarred overlying skin remained. Surgical removal of these masses would be difficult because of the fibrosis caused by the irradiation. With radium the treatment is prolonged, while with surgical methods it is brief and recovery is prompt. Figi also stated that radium treatment was not given over the chest of any of the patients with intrathoracic extensions. In my experience, high voltage roentgen therapy was of real value to a patient with mediastinal extension (case 9, fig. 47). Altogether, the experiences reported by Figi carry little support for the choice of radium in the treatment of hygroma.

I am inclined to use radium or, perhaps better, roentgen therapy in instances of extensive hygroma in children under 8 months of age, for whom radical removal is attended by great risk. Surgical removal might be reserved for a later time when the growth, as a result of ray treatment, had become smaller and possibly less vascular, rendering operation less dangerous. Irradiation should be used for an older child if the tumor is unusually large, making radical excision too hazardous. Ray treatment may be useful also after surgical excision, to prevent possible recurrence; I have not employed it in this series, in which there were no recurrences as far as could be determined. High voltage roentgen therapy is said to be as useful or more so than radium.

Radical surgical removal should be undertaken early, before the tumor has extended into the mediastinum or has involved important structures, such as the trachea, the large vessels and the nerve plexuses. Unusual technical difficulties are thus avoided and recurrences minimized. In the operation, a generous area of atrophic skin overlying the tumor is sacrificed. Subsequent satisfactory healing of the wound is thus assured. The nature of the growth and the penetrating character of its peripheral extensions make necessary a fairly wide excision. At times a margin of muscle, tendon or fascia, which may be incorporated in the wall of the growth, must be sacrificed.

The dissection at times is difficult because of the peripheral fibrosis and the adhesions by which the tumor is attached to the vascular sheaths in the neck and particularly to the jugular vein. These findings are probably accounted for by the early proximity of the cervical lymphatic sac and the jugular vein. However, it was possible in all the cases of cervical involvement except 1 to liberate the carotid artery, jugular vein and vagus nerve. In case 9 the tumor had completely incorporated these structures. It was necessary in 1 case to remove the contents of the submaxillary triangle in order to assure the complete removal of the tumor in the submandibular space (case 4).

It is important to preserve the tumor intact throughout the operation or at any rate as long as possible, in order to facilitate the dissection and thus assure complete extirpation. After puncture or slight rupture, the

fluid escapes and the mass is likely to collapse, losing the definition of its peripheral margins. In several instances the contour and distention of the hygroma were preserved by immediate suture of the puncture. Preliminary injection of methylene blue, as recommended by Da Costa, was not employed, for if the entire operative field becomes stained by leakage of the dye, extirpation of the growth becomes more difficult.

The thin, almost transparent cysts are usually readily liberated, whereas the older, fibrotic, adherent portions of the tumor require sharp dissection. A pedicle or cord of fibrous connective tissue, occasionally containing edematous lymph glands, was seen in a few instances extending downward in the neck and attaching itself to the jugular vein near or at its junction with the subclavian vein. In no instance was a communication with the vein found even after careful search and probing. At times the deeper portions of the cervical hygroma were firmly attached to the mastoid process, the base of the skull and the transverse vertebral processes.

After complete excision in these cases, wound healing was uneventful. In most cases the wound was closed without drainage; in others drainage was required for only a few days. The cosmetic result was all that could be desired, and the operative scars were almost invisible. In only 1 case was there a postoperative infection of the wound. This occurred after an operation for a recurrence of the tumor and was secondarily due to intercurrent acute coryza and sore throat. Culture from the wound yielded Streptococcus haemolyticus (case 10). Incomplete excision may, of course, be followed by recurrence (case 10). In another case infection present in the neck at the time of the operation was responsible for slow healing of the wound and prolonged drainage. Cultures taken from the throat and the operative wound showed the presence of Str. haemolyticus (case 9).

The operative results, except in the fatal case and in the case in which there was mediastinal involvement, were excellent. The mediastinal extension in the latter case prevented more than partial excision. After this, roentgen therapy proved to be of considerable benefit. Nitrous oxide with the addition of small amounts of ether was the anesthetic used in all the cases, except those of very young children, to whom ether alone was administered. The youngest patient operated on was 6 months of age. Four patients were aged 3 years or less. Five were over 20, and the oldest was 40.

Mortality.—The mortality among children suffering with hygroma, as previously reported in the literature, has been strikingly high, and this seems to have been true regardless of whether the therapy employed included no treatment, a minor surgical procedure such as aspiration or incision, radium treatment or surgical excision. Statistics on the mor-

tality of patients with hygroma are infrequent. An interesting statistical study reported in 1861, before the period of asepsis in surgery, is that of Storch,[5] who collected 24 cases from the literature. Puncture, incision, insertion of a hair drain, injection of iodine and extirpation were employed in a number of cases. The results were as follows: Ten patients recovered or were restored to health, 1 spontaneously and 9 as a result of the operative procedures instituted. Twelve died; 4 after too long-continued expectant treatment, 1 of pneumonia and 7 (6 of infection and 1 of "trismus") after operation. In 2 cases the effects were unknown.

Winslow [28] described 3 cases of cystic hygroma of the neck in infants and 1 case in which a diagnosis of hygroma had been made preoperatively but the growth proved at operation to be a lipoma. One of the 3 patients with hygroma died after operation. Winslow drew attention to the seriousness of the choice of treatment, for the prognosis may be doubtful after any form of therapy, including expectant treatment. Because of his experience, Winslow thought it would be good policy not to operate on children with hygroma unless symptoms, particularly of pressure, urgently demand intervention. When operation is indicated, excision should be done. Figi, as stated, reported a high mortality due to infection among his patients treated with radium.

In the tables prepared by Farr and reported by Dowd,[13] there were collected 91 cases of cervical hygroma and 35 cases of axillary hygroma. Eighty-two of the 91 cervical hygromas were subjected to various major and minor operative procedures, including puncture, incision, injection and partial or complete excision, with a fatal outcome in 39 instances. There was thus a mortality in this group of 47.5 per cent. Of the 35 axillary hygromas, 33 were subjected to similar procedures, with a fatal outcome in 5 cases, a mortality of 15 per cent. The average mortality in all the cases of hygroma in which operative treatment was given was thus 38 per cent.

There was 1 fatality in the present series of 12 cases, comprising 11 instances of radical and 1 of partial excision. The fatal case was that of a boy 6 months of age, with a hygroma which had been large at birth and had grown to a size considerably larger than his head (fig. 33). Death was attributable to shock secondary to the operative difficulties associated with the size, extent and vascularity of the tumor, rather than to the age of the infant. The operation was unusually extensive, and the child died eight hours after it. In the case of children under 6 or 8 months of age in whom a hygroma is very extensive, it is probably best, as previously stated, to employ radium or high voltage roentgen therapy. In view of the low operative mortality in this series, the

28. Winslow, R.: Cystic Hygromata and Other Tumors Occurring in Infancy, Surg., Gynec. & Obst. **25**:428, 1917.

objection to surgical removal because of its dangers does not hold. Surgical treatment in most cases is to be preferred over radium therapy. Not only the patients failing to respond to the irradiation but even those showing distinct improvement must be subjected to subsequent surgical measures if cure is to be obtained.

Ultimate "Follow-Up" Results.—Late results following excision of hygromatous tumors were observed in 5 instances (cases 1, 10, 9, 7 and 5). In 1 patient (case 1), a slight postoperative weakness of the left half of the lower lip was noted, but this had almost entirely disappeared ten months later. There was a slight residual numbness over the area of distribution of the cervical nerves. The operative scar was practically invisible. No glandular enlargements were noted, and the child was in excellent health. There was no evidence of recurrence.

The tumor recurred five months after the first operation in case 10. One year after the operation for recurrence, there was no further trouble. There was residual hemiatrophy of the right side of the tongue, the result of division of the hypoglossal nerve at the time of the first operation. There was no recurrence, and the cosmetic result was good.

In the third case (case 9), the hygroma after its partial excision was subjected to high voltage roentgen therapy, which was continued for a period of six weeks after the patient left the hospital. Two treatments per week were given. Repeated films taken of the mediastinum finally showed practically complete disappearance of the mediastinal extension of the hygroma (fig. 47). There was some persistence of the swelling in the right submaxillary space, where several enlarged lymph glands were palpable. These were possibly remnants of the old trouble. In other respects, the condition of the patient appeared favorable, and there was no definite evidence of recurrence fourteen months after partial excision and roentgen therapy.

Neurologic pressure symptoms, the pains radiating to the back of the neck and to the ear and the paresthesia of the head and fingers, were relieved at once by operation in case 7. The sensation of choking and difficulty in swallowing disappeared. The right arm occasionally became fatigued after considerable use. There was no evidence of recurrence after three years.

Several examinations following the operation revealed no recurrence in case 5; the last examination was made ten and one-half years after the operation. The pressure of the tumor had interfered with swallowing, breathing and speaking to an extent which the patient had not realized before the operation. The cosmetic result was pleasing to the patient.

In 1 instance (case 2) the operation had been done too recently when the patient was last seen for one to speak of the ultimate result.

One patient (case 3) died in shock after a too extensive operation.

COMMENT

A critical clinical and pathologic study of these 12 cases of hygroma has revealed the manner of growth and development of this tumor and has clarified its previously obscure power to penetrate and destroy anatomic structures that lie in its path. A review of the literature reveals that many different views have heretofore been held regarding the origin, the manner of growth and the peculiar destructive power of this tumor. Although hygroma is a relatively rare tumor, cases are not infrequently observed which illustrate its capability of causing extensive damage and even death. It is therefore desirable to have a clear conception of its true nature.

Since the publication of Wernher's studies,[1] hygroma has generally been considered a neoplastic formation, and its multilocular cystic character has been recognized. The conception that hygroma has a probable lymphatic origin gained support after the demonstration by Koester [9] that the cystic cavities were lined by endothelium. Thereupon its possible relation to lymphangioma was stressed by several authors (Borst [10] and Ribbert [15]), but it was conceded that the peculiar power of growth, penetration and destruction differentiated hygroma from lymphangioma. The most interesting and least understood features of hygroma which were previously observed concerned its manner of growth. Because of its similarity in some respects to lymphangioma, Borst [10] suggested that it might grow by a process of sprouting analogous to that in lymphangioma. Nevertheless, its power of penetration and destruction of adjoining tissues remained entirely obscure. It thus afforded a fascinating field for speculation as to its etiology and pathologic characteristics.

Failure to observe the characteristic histologic features of growing hygroma in the cases of previous investigators and in my earlier cases was due to escape of the fluid content of the hygroma at operation, causing the tumor to collapse. For observation of the true pathologic nature of the living tumor careful excision without rupture is essential. In my most recent cases, immediately on removal of the hygroma the contained fluid was withdrawn by means of a syringe and replaced with solution of formaldehyde. After the normally distended mass was thoroughly fixed, numerous blocks of tissue were taken from the growing margin for microscopic examination. The interpretation of the microscopic picture has afforded an adequate explanation for the growth of hygroma.

These histologic studies have demonstrated that hygromatous tumors grow, propagate and penetrate by proliferation and sprouting of endothelium and connective tissue from the walls of cysts in their growing edges. These sprouts, composed of fine endothelial fibrillae (fig. 17)

in the form of thin delicate membranes or streamers, grow out peripherally from the cyst walls. For a distance of 2, 3 or more millimeters they penetrate into the clefts of adjoining tissues, be they muscle, glands, blood vessels or nerves. Droplets of a lymphlike secretion similar to that in the adult cysts then arise within the fibrillae of the sprouts. This secretion is doubtless derived from the endothelial fibrillae themselves.

These droplets enlarge and cause the fibrillae to spread apart and canalize (figs. 19 and 20). In this fashion, new minute cysts with an endothelial lining acquired from the enclosing fibrillae originate. By continued secretion from the lining endothelium, these minute cysts grow to larger ones, and the fibrillae in the walls of these cysts continue distally into the adjoining tissues, to repeat the process. Fibrillar endothelial cords are seen to join the older cysts with the younger ones and to continue until lost in the more distant tissues, in a manner somewhat comparable to the growth of the banyan tree (fig. 17).

Examination of the zone immediately adjacent to the walls of the marginal cysts reveals constant microscopic attrition of the tissues as the hygroma eats its way, so to speak. Hygromatous stroma generally infiltrates this zone. A band of endothelial fibrillae, on meeting a tissue barrier, such as a small group of muscle fibers (figs. 9 and 10), divides to circumscribe and isolate it. The tissue thus isolated receives a covering of endothelial cells from the enveloping fibrillae. Between this cover and the peripheral fibrillae of the enveloping cord, a lymphlike secretion is formed from the endothelium, and in this manner a bundle of muscle fibers may be sequestrated in a newly formed cyst lined by endothelium. The encysted tissue, as a result of pressure and interference with nutrition, undergoes hydropic degeneration and fragmentation and finally disappears by solution in the surrounding fluid of the engulfing cyst. Confirmatory evidence of this solution is apparent in the study of the cyst fluid, which in many instances has been found to contain remnants of fragmented, fatty-degenerated cells, conglomerate nuclei and cellular débris.

Individual tissue units, such as a muscle fiber, may be circumscribed, isolated and destroyed without the intervention of an engulfing cyst (figs. 29, 31 and 32). The individual fiber, surrounded by endothelial fibrillae, undergoes hydropic and fatty degeneration. Small droplets of fat appear within the muscle fiber. These coalesce to form large globules and finally replace the whole fiber, which then takes on the appearance of true adipose tissue. Groups of fibers transformed into fat form distinct areas of adipose tissue, commonly seen in the walls of the larger cysts and in the adjoining tissues. This resolution into fat represents a replacement of normal tissues destroyed by the hygroma.

While this microscopic destruction of tissue is going on, the tumor simultaneously grows larger as it increases the pressure exerted by its walls, and the extension and penetration of the marginal cysts cause grosser damage to neighboring structures (figs. 13 and 14). Small cysts coalesce to form larger ones, and these in turn fuse after atrophy and disappearance of their intervening walls. In this manner the large cavities seen in the gross specimen of hygroma are formed. Whether the hygroma is quiescent, slow or rapid in its growth depends on the activity of these processes. The rapidity of growth occasionally seen has aroused a suspicion that it may be malignant, but nowhere in the reported cases or in my own have I seen any evidence of malignancy.

Grossly, the pressure of the larger thin-walled cysts may force the tumor in lines of least resistance into the planes or spaces between large muscles or vessels or even into the mediastinum. On meeting such a barrier, the cyst flows about it in saddlebag fashion and supplies it with an endothelial covering which is continuous with the lining of the surrounding cyst. A large anatomic structure, such as the sternocleidomastoid or pectoral muscle, may thus be related to the surrounding cyst as the testis is related to an enveloping hydrocele.

In view of these characteristics of the growth of hygroma, the belief of Thompson and Keiller and other recent writers is untenable. They are of the opinion that the extension of hygroma into neighboring regions is not due to an invasive power on the part of the endothelium. The appearance of hygroma in distant regions, such as the mediastinum, they conclude, is caused by cyst formation in lymphatic anlages occupying these regions. Apropos of the origin of hygroma, these studies have afforded support for the view that this tumor arises from lymphatic sequestrations from the primitive jugular sacs. Its manner of growth by a process of endothelial sprouting has some of the features characteristic of the development of the early lymphatic system and therefore accords with this theory.

In summary, the following are the principal factors in the origin, growth, propagation, penetration and destructive action of hygromatous tumors: first, the development of endothelial fibrillar membranes which sprout from the walls of the cysts and the penetration of these sprouts into surrounding normal tissues; second, canalization and cyst formation within these fibrillar sprouts by the secretion formed from the fibrillae themselves; third, the circumscription of tissue units by the endothelial fibrillae and their destruction either by primary hydropic or fatty degeneration or by sequestration and solution within the cysts newly formed about them, and fourth, the pressure exerted on the walls of the cyst by their fluid content and its transmission to surrounding tissues.

SUMMARY AND CONCLUSIONS

A detailed clinical and pathologic study of 12 cases of cystic hygroma is reported. In 10 of these the growth involved primarily the cervical region, and in 2, the axilla.

From a thorough review of the literature and a thoughtful consideration of the etiology of cystic hygroma, the plausible theory is that it arises from sequestrations of lymphatic tissue. In cases of cervical hygroma such sequestrations are derived from the primitive jugular sacs, which have failed to join the lymphatic system in the normal manner. Their potentiality of increasing in size to an almost unlimited extent is due to the fact that these "lymphatic rests" retain their embryonic power of irregular growth.

Predisposing or exciting causes are not known.

In the average case, there are no local or constitutional symptoms, although there may be cosmetic disfigurement. Symptoms may develop, however, in cases of advanced uncomplicated involvement, as a result of pressure on important structures, such as the trachea, pharynx and nerve plexuses. Severe respiratory embarrassment may occur when the tumor extends into the mediastinum. The large hygroma has a tendency to become secondarily infected, and the infection may be followed by serious symptoms or even death. Anemia and a poor nutritional condition are occasionally noted in children.

Hygroma is a benign, true neoplastic tumor of lymphatic origin. It is a multilobular, multilocular cystic tumor, the cavities of which are lined by endothelium characteristic of lymphatic spaces. The fluid content is usually clear or straw colored, occasionally turbid or blood stained. It is practically free of albumin or globulin and does not coagulate on standing. Various types of leukocytes, phagocytes, fragmented nuclei and cellular débris are noted in specimens which have been centrifuged; cholesterol crystals occur in cases in which there is hemorrhage. Lymphoid tissue, in fact, germinating centers, and possibly lymph glands are formed in abundance in cystic tumors.

Histologic evidence is offered as a basis for the explanation of the manner of growth, development and destructive action of hygroma. Endothelial fibrillar membranes or sprouts from the walls of the marginal cysts penetrate the adjacent normal tissues. A lymphlike fluid is secreted within the fibrillae, which are thereby caused to spread apart and canalize. Minute cysts with an endothelial lining are thus formed within these sprouts. By continued secretion within, the cysts enlarge; by pressure atrophy of the walls between adjoining cysts, the large cavities characteristic of hygroma are formed. The fibrillar membranes infiltrate and circumscribe adjacent tissues. Muscle fibers, nerves or other anatomic units are thereby sequestrated and destroyed, either by direct atrophy

and fatty degeneration or by being engulfed and disintegrated in the cystic fluid which is subsequently formed about them.

In the past, diagnosis has often been difficult and confusing, particularly with the more deeply situated tumors. They have been confused with lipomas, branchiogenetic cysts, hematomas, angiomas and tuberculous adenitis. When the true characteristics of these tumors are kept in mind, diagnostic errors should be relatively few. A positive clinical diagnosis can usually be made on the basis of the history and the physical examination.

Early treatment is advisable. Minor surgical procedures sometimes adopted include aspiration, simple incision for drainage and injection of sclerosing substances. Such procedures are futile in view of the multilocular nature of the tumors and the great danger of secondary infection with severe sepsis. Irradiation has been practiced in the past with indifferent results. For very large tumors in children under 6 or 8 months of age, irradiation preliminary to surgical treatment is desirable. Secondary surgical excision, however, is still necessary for cure.

Radical surgical excision is by all odds the treatment of choice.

There was but 1 fatality in this series, although the mortality after surgical removal of hygroma has been rather high in the past. The immediate and ultimate results were excellent cosmetically and as regards complication.

In 1 case there was a recurrence of the growth five months after the first operation. Late results following operation for hygroma were observed in 5 instances over periods of ten months to ten and a half years. In a case of partial excision of a hygroma which was subsequently treated by high voltage roentgen therapy, the patient, a child, was in good condition fourteen months after operation. In the remaining 5 cases the immediate result was satisfactory but a late "follow-up" was not possible.

REPORT OF CASES

CASE 1.—G. S., a girl aged 9 years, was admitted to the Long Island College Hospital on June 26, 1932, because of a tumor on the left side of the neck. She was discharged on July 2.

History.—The family history and the past history of the patient were unimportant. Two years previous to the child's admission, when she was 7 years of age, a small soft swelling appeared below the angle of the jaw on the left side of the neck. The child was said to have been kicked at the site of the tumor some months previously. Six months after it was first noticed, the tumor was as large as a medium-sized orange. There had been no increase in growth in the past one and one-half years. A tuberculin test done about a year previous to admission had given negative results. The tumor was examined by Dr. A. L. L. Bell on April 21, 1931, and he believed it to be an angioma. On Dec. 5, 1930, the child was examined in another clinic, where the diagnosis of tuberculous adenitis was made. Von Pirquet's test, aspiration and roentgen therapy were advised.

Examination.—The swelling on the left side of the neck (fig. 3) measured 8 cm. in the longest oblique diameter and 5.5 cm. in transverse diameter. It was as large as a medium-sized orange and presented a rounded, domelike swelling which occupied the region between the tip of the mastoid process and the angle of the jaw. The swelling extended down under the sternocleidomastoid muscle to the middle of the neck. The overlying skin was not attached. The swelling was soft and fluctuant, giving the impression of being filled with fluid. On pressure over the anterior portion of the tumor, there was a noticeable bulging immediately behind the posterior border of the sternocleidomastoid muscle. At the lower pole of the tumor, an enlarged lymph gland the size of a lima bean was felt; the mass was not tender. The swelling extended anteriorly almost to the midline. During forced expiration or movements of the head to the left against resistance, the tumor increased somewhat in size, while the left external jugular vein distended definitely and much more than the right. The tumor transilluminated well. The thyroid gland was barely palpable. The erythrocyte count was 3,200,000, the hemoglobin content 65 per cent and the leukocyte count 6,800. There were 65 per cent polymorphonuclears, 30 per cent small mononuclears, no large mononuclears, 3 per cent eosinophils and 2 per cent transitional cells. The urine was normal. The preoperative diagnosis was hygroma of the left side of the neck.

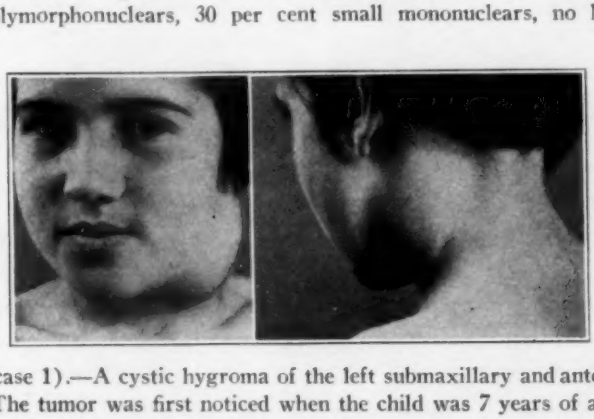

Fig. 3 (case 1).—A cystic hygroma of the left submaxillary and anterior cervical triangles. The tumor was first noticed when the child was 7 years of age. It grew rapidly in the beginning and later became quiescent. The hygroma extended from the mastoid process across the submaxillary triangle to the midline and downward almost to the sternoclavicular joint. It was firmly adherent to the vascular sheath, contained many thin-walled cysts filled with straw-colored, watery fluid and was associated with groups of hyperplastic lymph glands.

Operation.—The hygroma of the left side of the neck was excised on June 27 with the patient under light chloroform and ether anesthesia. A horizontal incision was made on the left side of the neck 1 inch (2.5 cm.) below the angle of the jaw and over the most prominent part of the tumor. The greatly distended external and anterior jugular veins were ligated and divided. The surface of a thin-walled, cystic tumor giving a bluish reflex was uncovered and separated from the surrounding tissues, to which it was everywhere rather firmly adherent. The sternocleidomastoid muscle was gradually stripped away, and the tumor was outlined by careful blunt dissection. The tumor was situated under the sternocleidomastoid muscle and projected into the posterior triangle, upward almost to the mastoid process and forward and upward into the submaxillary triangle, anterior to the thyroid cartilage and hyoid bone. It thus occupied the greater portion of the

anterior triangle and extended downward to approximately 1 inch (2.5 cm.) above the sternoclavicular joint. The tumor was firmly adherent to the digastric muscle. The dissection was carried to the posterior-inferior surface, where the tumor was firmly adherent to the vascular sheath and particularly to the internal jugular vein. The lower pole of the tumor was adherent to a group of eight or ten lymph nodes as large as lima beans and situated in the posterior triangle. The lower pole with this group of glands was dissected free. The tumor was then liberated in an upward direction. This procedure exposed the carotid artery and the internal jugular vein. The upper pole was loosely attached to and readily freed from the tissues of the submaxillary triangle. There was clearly no stalk or other intimate connection with either the internal jugular or the subclavian vein. The wound was closed without drainage.

Postoperative Course.—July 2 1932: Convalescence was uneventful, and the wound healed per primam intentionem. A slight stiffness of the neck was noted.

Gross Pathologic Examination.—The tumor was as large as a medium-sized orange, encapsulated and multilocular. The walls of the cysts were thin, membranous and semitransparent. The cystic character and the spongy consistency of the tumor were apparent on section. The lining of the cysts was smooth and glistening. A group of lymph nodes, each measuring 0.5 to 1 cm. in diameter, was incorporated in the mass. The fluid in the nodes was thin watery and faintly straw colored and showed crystals of cholesterol on its surface. (Blocks of tissue were taken from the walls of the cysts, from the collapsed spongy tumor and from the attached lymph glands.)

Examination of the Cyst Fluid.—On microscopic examination the fluid from the cyst was found to contain numerous lymphocytes, some phagocytes, polymorphonuclear cells and a large number of cholesterol crystals. Large phagocytes, about three to eight times the diameter of the lymphocytes, contained numerous large refractile, yellowish brown granules resembling hemosiderin crystals.

Microscopic Examination.—Four blocks of tissue were taken from representative portions of the specimen received in the laboratory. Representative sections of the blocks are here described.

Block III, Section *d*. Low Power: This section represented a mass of tissue enclosing a portion of a partially collapsed cyst lined by endothelial cells (fig. 4). In the subendothelial zone there were small lymphoid aggregations and true follicles with germinating centers. Below this there was a zone of connective tissue, consisting of small and large meshy fibrillae. Still farther away from the lumen, areas of fine areolar tissue could be seen. Finally the bulk of the tissue was made up of a loose, spongy connective tissue ground substance in which were seen well defined, hyalinized fibrillae of connective tissue in loose arrangement and areas of endothelial cell growth in the form of streamers, in which occurred numerous small capillaries and lymph vessels. A papillary projection into the cyst contained numerous lymphoid follicles, which appear as dark areas in figure 4.

Medium and High Power: One striking and interesting portion of the section showed a papillary projection into a cyst space. At the base was a peculiar area composed of cell cords or columns enclosing elongated, slitlike spaces. The nuclei were large and chromatic. The nature of this area was entirely obscure. The papillary projection had a ground substance or stroma of loose, fine and coarse fibrillar connective tissue in which occurred accumulations of lymphoid cells, rich in blood capillaries (fig. 5). A few of these areas had advanced to the formation of definite follicles with germinating centers. The stroma was composed

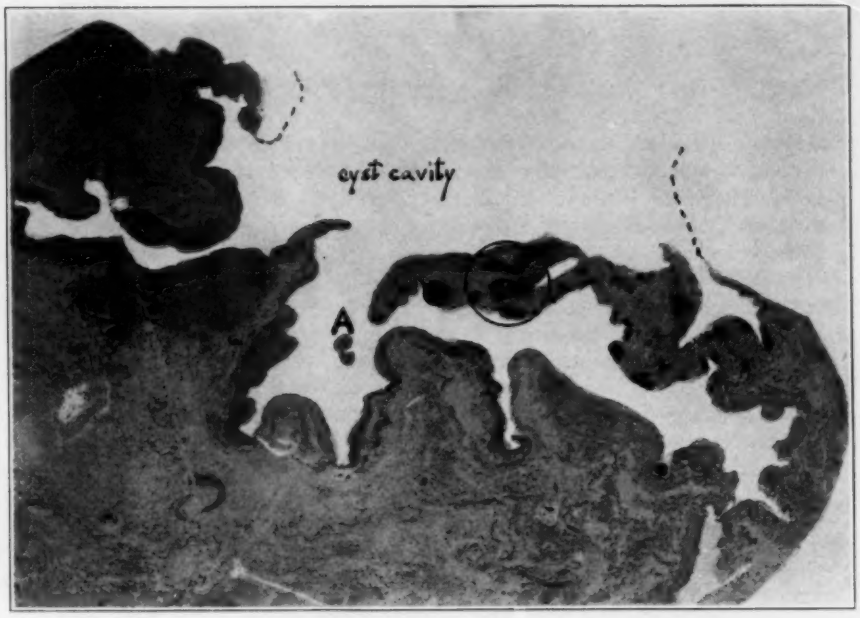

Fig. 4 (case 1).—A low power photomicrograph (× 6) of a section of a hygromatous stroma which forms the wall of a partially collapsed cyst. On the right is seen an intracystic papillary process containing dark aggregations of lymphoid cells and follicles. The bodies in the center, *A*, represent two occluded arteries. They have persisted as trabeculae traversing the cavity of the cyst after the partition in which these arteries were confined had disappeared as a result of pressure between two adjoining cysts.

Fig. 5 (case 1).—A photomicrograph (× 50) of the area enclosed in the circle in figure 4. Numerous dense aggregations of lymphoid cells, often the antecedents of true lymph follicles, are shown, together with numerous small blood vessels. Note, toward the right, the peculiar structure consisting of cell cords with intervening slits, the nature of which is not clear. This area is shown in higher magnification in figure 6.

largely of foamy areolar tissue which was almost devoid of cells. Transitions could be seen from the numerous small aggregations of lymphoid cells to the well defined lymphoid follicles. In addition to the lymphoid cells, there were large numbers of plasma and epithelioid cells. Numerous small vessels were visible. There was an abundance of loose, delicate, foamy areolar reticular tissue, the cells of which sent out delicate processes, anastomosing with each other to enclose small clear spaces. The nuclei were small and oval.

In the larger aggregations of lymphoid cells, there were definite hyperplastic germinating centers. In these centers appeared commonly very large cells with scant protoplasm and with huge, pale-staining, irregularly shaped, oval or rounded nuclei, nuclei intermediate in size and finally cells of lymphoid and epithelioid types. Occasional karyokinetic figures were seen. These germinating centers were sur-

Fig. 6 (case 1).—A high power photomicrograph (× 400) of the area of cell columns shown in figure 5. Note the discrete cell cords enclosing elongated slit-like spaces and the numerous large hyperchromatic nuclei. The significance of this structure is not clear.

rounded by a dense zone of lymphoid cells. The entire follicle was not unlike that seen in the hyperplastic lymph glands described elsewhere (figs. 11 and 12). The cell cords and the slitlike spaces (fig. 6) were not lined by definite endothelium. The protoplasm of the cells in the cords had a somewhat foamy, delicate appearance. The nature of this structure is obscure.

The papillary projection (seen in low power in figure 4) was lined by typical endothelium. The ground substance of the whole process was made up of very fine, areolar, reticular connective tissue alternating with more dense, pink-staining fibrillar connective tissue, in the meshes of which occurred numerous small capillaries, a sprinkling of lymphoid cells and numerous fairly large pink-staining plasma cells.

Opposite this papillary projection was found a thick wall lining the cyst. It appeared older, as was indicated by the rather broad zone of fibrillar, pink-staining connective tissue of hyaline type seen in low power in figure 7. The wall was lined by typical endothelium. In this thick wall of connective tissue were numbers of cells of the lymphoid, epithelioid and lymphoblastic type.

Below this dense connective tissue wall was a zone composed of a meshwork of loose areolar fibrillae and numerous small vessels. There was evidence of a rich proliferation of endothelium, which was forming small capillaries and lymph spaces (fig. 7).

Lying free in the cyst cavity were two rounded, isolated bodies which had an endothelial lining (figs. 4 and 8). The outer zone of each was composed of dense concentric layers of hyaline fibrillar connective tissue, and in the center of

Fig. 7 (case 1).—A low power photomicrograph (× 60) of the wall of the cyst shown in figure 4. Note the endothelial lining, the thick hyaline connective tissue wall and below this a broad zone of delicate, fine fibrillar structure characteristic of the stroma of hygromatous tumors.

each there was a core of organized hyaline fibrous tissue, in which were seen a few small lymphoid connective tissue cells and the pale pink-staining lymphoblastic cells. Their outer surfaces were lined by endothelium. These bodies were interpreted as cross sections of trabeculae coursing through the cyst cavity, resulting from organization of thrombosed arteries persisting after atrophy of former cyst partitions.

Block III, Section *h*. Medium Power: This section, taken from an area adjoining a large cyst, showed the separation and isolation of muscle fibers produced by the ingrowth of endothelial fibrillar tissue. Many of the muscle fibers were atrophic and showed hydropic degeneration and beginning disintegration. A small cyst was seen, lined with endothelium which continued as a fibrillar streamer

upward and to the right (fig. 9, × 175), enclosing a nerve fiber (*N*). A cystic space was forming around the nerve. The small cyst was filled with fluid, isolated in which was a muscle bundle composed of four or five muscle fibers which were themselves surrounded on their external surface by endothelium. The delicate fibrillar stroma is seen in the upper part of the photomicrograph.

High Power: The small muscle bundle enclosed in the cyst was composed of four or five fibers which showed evidences of degeneration, and which were separated from one another by a few small fibrillae with endothelial-appearing nuclei (fig. 10, × 320). The bundle itself was completely surrounded by a single layer of endothelial cells. This bundle lay isolated in an irregular oval space containing a blue-staining, foamy coagulated lymph in which there were several small trabeculae of endothelial cells. This space or cyst was lined by endothelium and a thin layer of fibrillar subendothelial connective tissue. A fine fibrillar

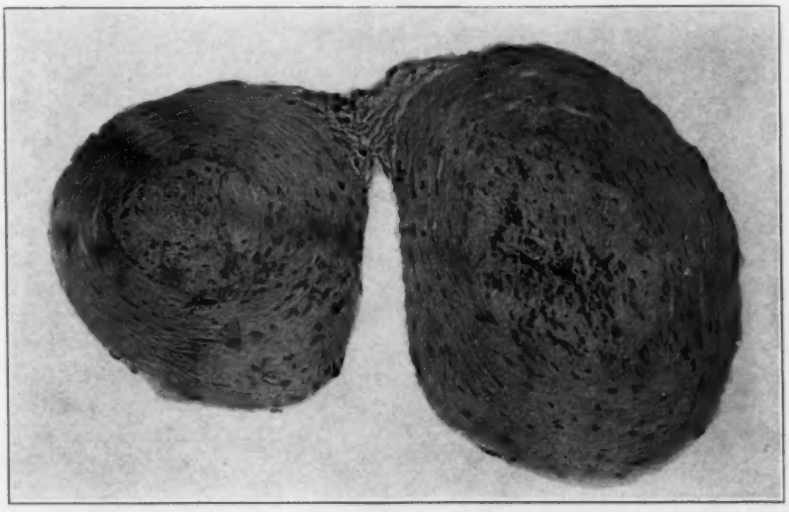

Fig. 8 (case 1).—A photomicrograph (× 150) of cross sections of trabeculae traversing a cyst cavity (cf. *A* in low power, figure 4). Such trabeculae, commonly seen in hygromatous tumors (fig. 14 *A*, III), represent blood vessels which formerly ran in the walls between adjoining cysts, and which have undergone thrombosis and organization. After pressure atrophy and disintegration of the cyst walls, these vessels persist as isolated cords. Note the peripheral concentric hyalinization, the central organization and the external covering of endothelium.

endothelial sprout, continuous with the endothelium of the cyst, continued upward to the right and completely enclosed a nerve fiber (*N*, fig. 9) in a thin layer of fibrillar tissue, in which fine, spindle-shaped endothelial cells could be seen. There was a space between the nerve fiber and the enveloping endothelial capsule which suggested the presence of coagulated lymph. Fibrillar endothelial tissue was seen running between muscle bundles and even penetrating between the individual muscle fibrillae. Between the fibrillae of this endothelial tissue could be seen a bluish, foamy secretion much as in the cyst space itself. (This was interpreted as coagulated secretion derived from the endothelial cells.) Many of the muscle fibers were poorly stained and appeared swollen and hydropic, while others appeared fairly normal.

In one area of the section, embedded in the spongy stroma, there was an isolated bundle of muscle fibers, of which some were swollen, pale staining and hydropic in appearance while others showed fragmentation of the fibrillae. The resulting fragments were homogeneous and glassy in appearance and had lost their affinity for stain. Surrounding and separating these fragments was the fibrillar connective tissue stroma.

Block III, Section *i*: This section represented an area much like that represented in section *h*. It showed very well the infiltration of the endothelial tissue between and around a small bundle of muscle. This bundle, similarly, lay sequestrated in a cystic space. It showed well the gelatinous hydropic degeneration of muscle fibers, around which there was seen the characteristic fibrillar, endothelial tissue, as in section *h*.

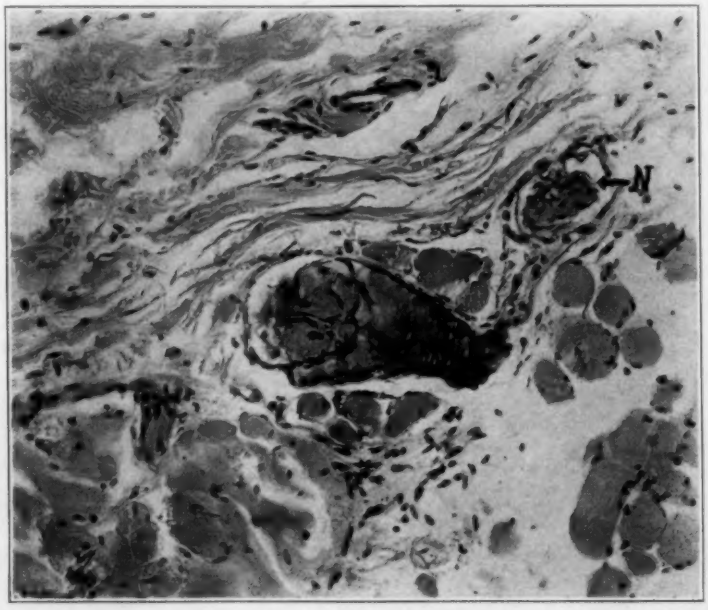

Fig. 9 (case 1).—A photomicrograph (× 175) of an area adjoining one of the larger cysts. The section shows in its upper half the delicate fibrillar stroma and in its lower half bundles of muscle separated by the penetration of endothelial fibrillae. Many of the muscle fibers show evidences of degeneration. In the center is a small cyst enclosed in an endothelial envelop and containing dark-staining (hematoxylin) lymph. The cyst has completely surrounded and engulfed a bundle of muscle fibers, which are covered with endothelium and which lie free in the lymph. Note, at the right extremity of the cyst, a sprout of endothelial fibrillae continuing upward to enclose a nerve fiber, *N*. A small newly formed perineural cystic space is seen.

Block II, Section *a*. Low Power: The section, a longitudinal cut of a large lymph gland, showed a thick cortical zone and a relatively small hilus (fig. 11, × 7). The gland measured 1.3 cm. in longest diameter. Throughout the thick cortex were dense accumulations of lymphoid cells. In the hilus were large lymph spaces filled with lymphoid cells and numerous small blood vessels. The

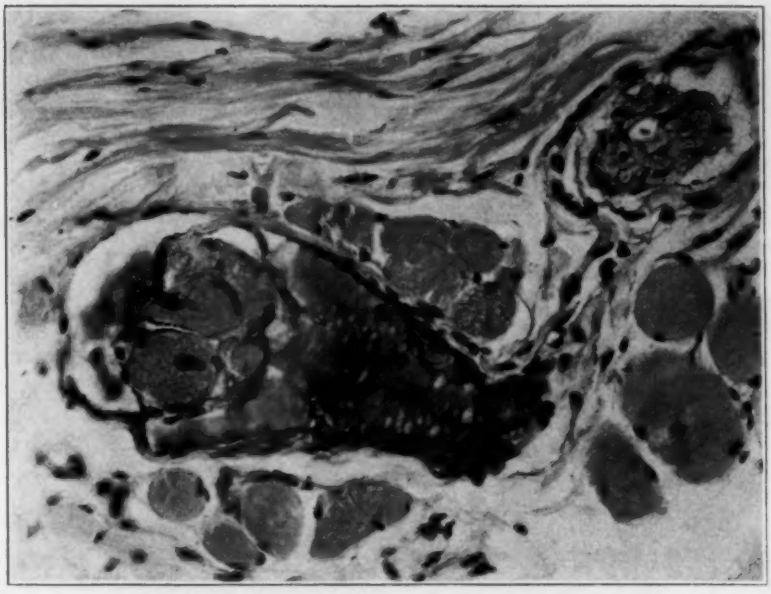

Fig. 10 (case 1).—A photomicrograph (× 320) of the cyst and adjoining area shown in figure 9. Note the endothelial lining of the cyst, the dark-staining lymph and the sequestrated muscle bundle, on the surface of which a single layer of endothelial cells is seen. The muscle fibers show evidences of hydropic degeneration. The endothelial streamer, which is derived from the cyst wall, continues upward and divides to enclose a nerve fiber. Note the formation of a new perineural cyst. In the hygromatous stroma are several muscle bundles. Some of their fibers are fairly normal in appearance; others show beginning fragmentation, and those in the right lower field have undergone almost complete solution.

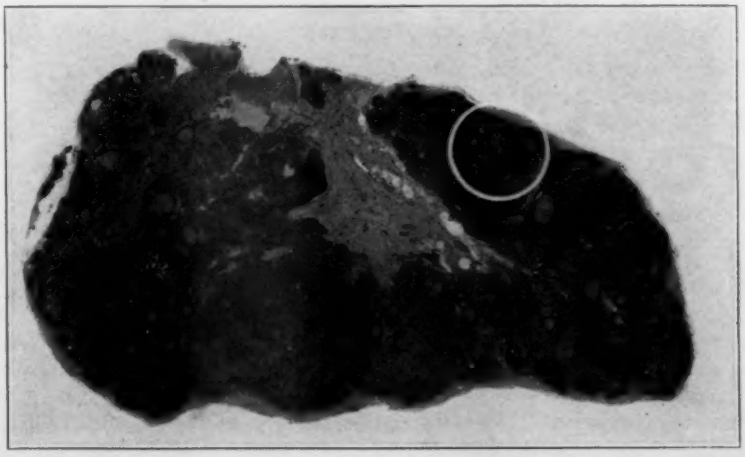

Fig. 11 (case 1).—A photomicrograph (× 7) of a longitudinal section of a large hyperplastic lymph gland from the tumor shown in figure 3. Attention is called to the dense zone of lymphoid cells and the numerous large lymphoid follicles occurring throughout the cortex. This picture is typical of what is seen in the lymph glands occurring in intimate association with a hygromatous tumor.

striking feature of the cortical portion of the gland was the large number of lymphoid follicles with germinating centers. In the peripheral zone of the cortex the follicles were particularly large. The appearance was that of a hyperplastic lymph gland.

High Power: The germinating centers in this lymph gland had in general the same appearance as that described for the lymph follicles in the papillary projection (figs. 4 and 5). The cell types were essentially the same, namely the lymphoblastic, intermediate and lymphoid cell types (fig. 12). Furthermore, there were the large epitheliod cells and those resembling the endothelial type. There was a striking frequency of karyokinetic figures. A number of small capillaries were seen. There was a dense outer zone of lymphoid cells together with groups

Fig. 12 (case 1).—A photomicrograph (× 50) of the area enclosed in the circle in figure 11. Note the large lymphoid follicles and the dense aggregations of lymphoid cells. Numerous lymphoblastic germinating cells with karyokinetic figures have been noted, not only in the follicles of the glands associated with hygroma but in the localized aggregations of lymphoid cells independent of true lymph glands. There is evidence that hygroma has the potentiality of producing isolated germinating follicles in all respects similar to those seen in lymph glands.

of pale-staining epithelioid cells, some lymphoblastic cells and numerous small capillaries. Endothelium was also seen, apparently forming new, small capillaries.

The hilus contained, besides the blood vessels and groundwork of connective tissue, large lymph sinuses, some of which were entirely filled with lymphoid and lymphoblastic cells and a few of epithelioid type. Plasma cells were frequent. Large blood spaces were also common. The appearance was that of a definitely hyperplastic lymph gland. Polymorphonuclear cells were hardly noted. The diagnosis was hygroma colli cysticum.

Follow-Up Note.—May 4, 1933: Ten months after operation, the child was found to have been in excellent health. A linear scar was seen on the left side of her neck. There were no swellings visible or palpable. The cervical glands on either side were not enlarged. (For a time after operation there had been a weakness of the left half of the lower lip which produced a definite asymmetry of the mouth.) At the time of this examination there was only the slightest evidence of this condition when the patient forcibly grinned. There were slight numbness and hyperesthesia over the region of distribution of the upper cervical nerves. No evidence of recurrence was found.

The pulse rate was 84 and the weight 65½ pounds (29.7 Kg.).

Case 2.—H. F., a white boy aged 3 years, was admitted to the Long Island College Hospital March 13, 1933, because of a tumor on the right shoulder and upper part of the right arm.

History.—The patient was born at full term, labor being spontaneous. He walked at the age of 1 year. At the time of admission he talked little; and speech was indistinct. His mental development had been somewhat retarded. At the age of 3 weeks, a mass the size of a walnut was noticed on the upper part of the arm. The tumor gradually grew larger until it was approximately the size of a grapefruit. It had not been painful or inflamed, nor had it interfered, except by its weight, with the movements of the arm. The history with reference to the various systems of the body revealed nothing abnormal.

Examination.—The facial expression was rather dull, and occasionally there was drooling of saliva. The patient breathed through his mouth and had the typical adenoid facies. He appeared underweight and somewhat below par. The child was moderately hydrocephalic in appearance; the fontanels were almost completely closed; the tonsils were hypertrophic, and the pharynx was mildly injected. The abdomen was somewhat full, protuberant and soft. General examination gave negative results. The child's extremities were well developed. An oval mass was seen overlying the upper part of the right arm from the shoulder joint downward almost to the fold of the elbow (fig. 13). It was about the size of a grapefruit. The skin over the greater part of the anterior surface was thin and mottled. The tumor was sessile and could be freely shifted from side to side, but it could not be moved on its base, which seemed to be attached to the humerus. It measured in longitudinal diameter 16 cm. and in transverse diameter 10 cm. The circumference of the arm and tumor was 29 cm. It had a definitely soft, fluctuant feel but was not tender. The tumor transilluminated well. It was not attached to the overlying skin. In the substance of the tumor could be felt small indurations and firm trabeculae. The upper pole reached the border of the pectoralis major muscle and possibly extended beneath it. It overrode the upper surface of this muscle for a short distance. The base of the tumor overlay the humerus, the surface of which had a definitely irregular contour. The pulsations of the axillary artery were readily felt below the lower posterior margin of the tumor. There was no apparent atrophy of the right arm, and movements of the arms were about equally well performed.

The temperature was 100 F., the pulse rate 100 and the respiratory rate 23. The systolic blood pressure was 106 and the diastolic 65. The erythrocyte count was 4,000,000, the hemoglobin content 65 per cent and the leukocyte count 8,400. There were 32 per cent small mononuclears and 10 per cent large mononuclears; no abnormal cells were found. The examination of the urine and the Wassermann and Kahn tests gave negative results. The preoperative diagnosis was hygroma of the upper part of the right arm.

Operation.—The hygromatous tumor was excised on March 29, with the patient under nitrous oxide anesthesia. The cystic tumor was punctured, and about 20 cc. of a light brownish red, moderately turbid fluid was withdrawn. The incision was begun from a point immediately in front of the shoulder joint, extended downward medially and laterally to include a large lenticular area of skin, and continued almost to the fold of the elbow. Skin flaps were freed medially and laterally with great care in order to avoid rupture of the thin, bluish, transparent cyst walls. On the medial aspect, it was found that a thin layer of muscle derived from the biceps and brachialis anticus muscles was spread out over the tumor. A portion of muscle was allowed to remain adherent to the mass. The intercostal humeral nerves were sacrificed. The tumor was firmly attached to the lateral margins of the bicipital groove. These adhesions were liberated, as was a portion of the insertion of the pectoralis major muscle. The tumor did not extend into the axilla or along the great vessels, which were fully exposed. The limiting walls

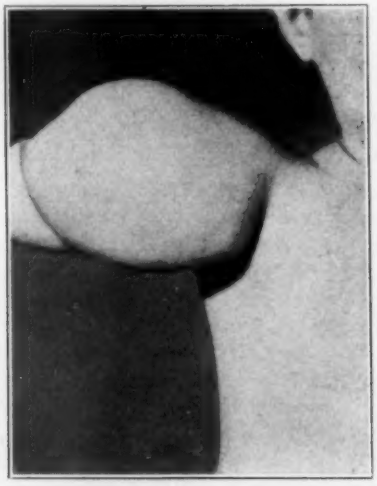

Fig. 13 (case 2).—A photograph of a cystic hygroma of the right shoulder and upper part of the right arm of a boy 3 years of age. The hygroma was first noticed when the child was 3 weeks old, and it was then as large as a walnut. It enlarged progressively and reached the size of a grapefruit in three years. At the time of the operation it measured 16 cm. in length and 10 cm. in transverse diameter. Cystic prolongations of the tumor had penetrated and destroyed a large portion of the deltoid muscle. There were no symptoms, but the sheer weight of the tumor interfered with movements of the arm. A photograph of the gross specimen is shown in figure 14 *A* and *B*.

on the inferior aspect of the tumor were then easily freed from the humerus. Laterally, the margin of the triceps muscle came into view. The cysts were found to continue onward into the substance of the deltoid muscle (fig. 14 *A*, VI and VII). There were several finger-like, multicystic prolongations, penetrating and separating the muscle bundles in the anterior half of the deltoid. Consequently, in order thoroughly to eradicate this portion of the tumor, it was necessary to detach and excise the clavicular portion of the deltoid muscle. The upper limits of the hygromatous tumor did not appear to extend beyond the origin of the deltoid

muscle from the clavicle. Two or three punctures were made; but these were immediately closed with fine silk, and the tumor was preserved in toto.

Examination of Fresh Specimen.—A section of the thin wall of the tumor was removed. A large amount of fluid, as previously described, escaped. The cavity of the cyst was subdivided into several large and small recesses. The glistening inner lining was generally smooth and trabeculated, and some firm partitions were seen. The opening was sutured with fine silk and the tumor was distended with solution of formaldehyde to its former natural size. The inner lining of the thin cyst wall was studied after treatment with silver nitrate, which was reduced in the sunlight. The endothelial nature of the lining is clearly shown in figure 15.

Examination of Fresh Fluid Removed from the Cystic Tumor (Dr. Albert Ritzmann).—The fluid obtained by aspiration of the tumor appeared light brownish red and moderately turbid. Agitation displayed many tiny refractile, shiny particles, resembling cholesterol crystals. It did not coagulate. A centrifuged specimen showed a clear, light golden supernatant fluid and a small amount of reddish, granular sediment. A smear of the original fluid, treated with Wright's stain, showed many achromic red blood cells, slightly larger than normal. Many degenerated cells and small lymphocytes, together with occasional granular, large (15 microns) phagocytes were also seen. The latter were filled with yellowish granules, resembling hemosiderin. A considerable amount of amorphic, granular, cellular débris was seen. The unstained smear showed, in addition to these structures, a considerable number of cholesterol crystals. The clear supernatant fluid contained perhaps both albumin and globulin elements, since both the concentrated ammonium sulfate and the nitric acid ring test gave a thick whitish layer. Heating brought forth a similar coagulated material. The erythrocyte count was 42,500 per cubic millimeter.

Postoperative Course.—April 24, 1933: The patient made an uneventful recovery. The wound was well healed.

Gross Pathologic Examination.—The specimen was a cystic lobulated tumor which had been distended and partially fixed by the injection of solution of formaldehyde into the cystic cavities soon after its removal. The superior surface of the tumor was covered by a thin, atrophic, semitranslucent skin. The inferior surface showed small and large cystic lobulations and prominences (fig. 14). The tumor measured 12 cm. in longest longitudinal diameter and 10.5 cm. in transverse diameter. At its upper extremity, there was a section of muscle which was intimately attached to the upper pole of the tumor and which had, in part, been invaded by the cysts. The surface of the cystic lobules was covered in places with a heavy, thick white fibrous connective tissue. In other areas, the walls were extremely thin and transparent. The tumor was placed in solution of formaldehyde.

After thorough fixation of the specimen, its inferior wall or base was cut away from the tumor proper and elevated in the manner of a lid, the interior (fig. 14 *A* and *B*) of this cystic mass thus being exposed. This comprised an irregular space the size of a large orange. There was a heavy, dense limiting wall of white fibrous connective tissue from which thick and thin trabeculae and partitions radiated into the interior of the tumor, dividing it into numbers of small and large irregularly cystic spaces. The inner wall was everywhere trabeculated and lined by a glistening, pearly white membrane resembling endothelium. At the upper pole could be seen a series of cysts, which had penetrated a large muscle (representing a portion of the deltoid muscle [fig. 14]). The smaller cysts were surrounded by muscle bundles which had been separated by the growth and penetration of the cysts and which had been incorporated in the walls and trabeculae between

the cysts (fig. 14 *A*, VII). Finally, the atrophic muscle fibers disappeared in the deeper, older portions of the tumor. A portion of this muscle had been definitely caused to atrophy by penetration and pressure of the cysts (fig. 14 *A*, VI and VII). One isolated cord or trabecula was seen enclosing a blood vessel of fair size containing a blood clot (fig. 14 *A*, III).

Microscopic Examination.—Blocks were taken from representative areas indicated by the numerals in figure 14 *A*, and sections prepared for microscopic examination.

Block II: A section from this area represented an area of tumor stroma of characteristic appearance. It lay between masses of muscle fibers. Strands or shoots of endothelial and connective tissue fibrillae were seen insinuating themselves between the muscle bundles. A serpentine cord of typical endothelial fibrillar tissue was seen coursing through the middle of the section. This cord or streamer

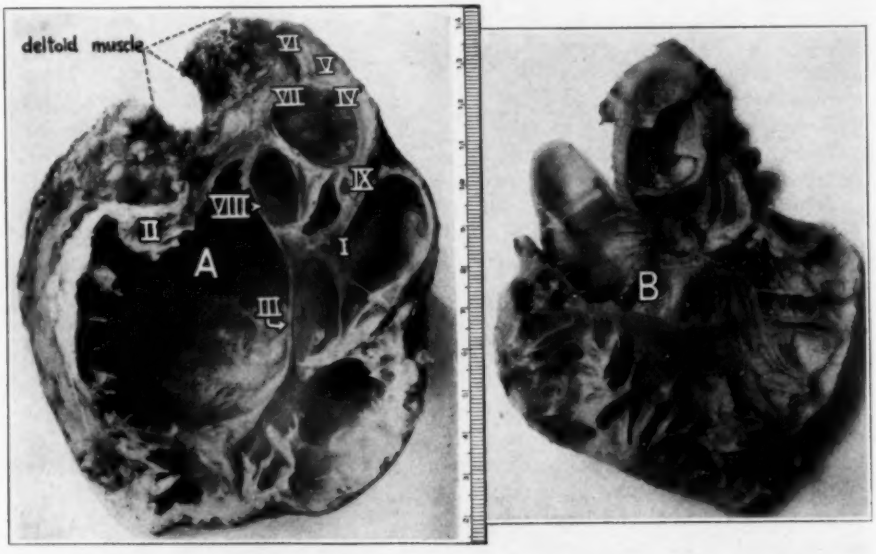

Fig. 14 (case 2).—*A*, the interior of the cystic hygroma shown in figure 13. *B*, the internal surface of the inferior wall or base of the tumor. The tumor, measuring 12 by 10.5 cm., was distended to natural size with solution of formaldehyde immediately after its removal in order to preserve the characteristics of the living tumor. Note in *A* the multilocular character of the cystic mass, the thin-walled and thick-walled cysts, some of which are intercommunicating, the remnants of the former partitions, the trabecula which contains an artery (area III) and the section of the deltoid muscle invaded by cysts (areas VI and VII). Note in *B* the inner surface of the base, showing perforated partitions, trabeculae and diverticula produced by the pressure of the cysts. The tumor contained a large amount of light brownish red turbid fluid.

was composed of a meshy, fibrillar stroma enclosed in endothelium. Within this cord were numerous small capillaries and cells of various types, recognized as endothelial, lymphoid, epithelioid and large mononuclear cells.

Block III: This area yielded a cross section of a trabecula which traversed the cyst cavity. It is visible in the photograph of the gross specimen (fig. 14 *A*,

III). A blood vessel was enclosed within its walls. (This vessel undoubtedly acted as a splint to preserve this isolated fine trabecula.) The walls of the trabecula had the structure common to the walls of the cysts.

The Lining of the Cysts: Immediately after the tumor was removed, the cystic cavity was opened, and flat sections were stripped from the lining and treated with a 3 per cent solution of silver nitrate. Thereupon the sections were exposed to the sunshine and the black silver salt was precipitated in the cement lines of adjoining cells. The reduced silver thus outlined the lining endothelial cells in the manner of a mosaic. Microscopically, this revealed a single layer of

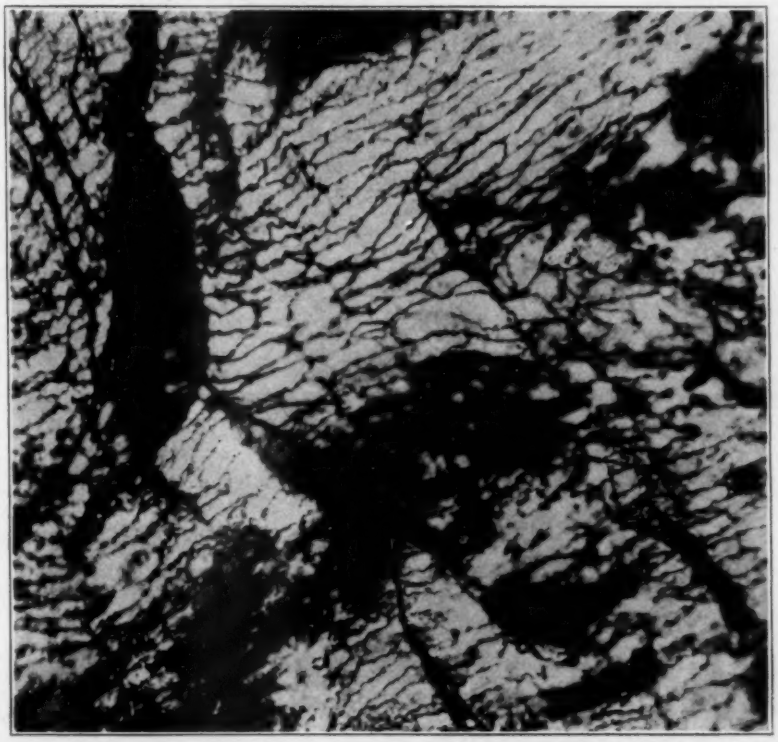

Fig. 15 (case 2).—A flat section of endothelial lining of a cyst from the hygroma illustrated in figure 14 *A*. The specimen was flattened on a slide and treated with a 3 per cent solution of silver nitrate, which was reduced by sunlight. The reduced silver salt, by its precipitation in the intercellular substance, outlined clearly the lining cells. They resemble the characteristic appearance of the endothelial cells lining the lymph and blood vessels. (High power.)

surface cells, which were elongated, hexagonal and characteristic of the lining endothelium of blood and lymph vessels, not of the mesothelial lining of connective tissue cavities, such as joint cavities or bursae. This demonstrated the endothelial nature of the lining of the hygromatous cysts (fig. 15).

Block I: A section from this area (fig. 14 *A*, I) represented the wall between two adjoining cyst cavities. The wall had the usual endothelial lining, below which was seen a zone of loose, meshy, fibrillar reticulum, containing numerous small

blood vessels, lymph sinuses and accumulations of lymphoid cells. Running along in the center of the wall was a band of muscle fibers, which were compressed between the adjoining cysts, and which showed evidences of atrophy and hydropic degeneration. Areas of young connective tissue were seen, in which could be recognized newly formed capillaries, and the characteristic endothelial fibrillar tissue.

Block VIII. Low Power: A section (fig. 16) from area VIII (fig. 14 *A* and illustrated in fig. 16) showed the very delicate structure of one of the thin cyst walls, lined by endothelium on the outer surfaces and composed of loose, spongy stroma consisting of reticular, areolar, fibrillar connective tissue in which were

Fig. 16 (case 2).—A photomicrograph (× 50) of a representative section of a thin cyst wall (area VIII, fig. 14 *A*). Note the spongy stroma, the dense aggregations of lymphoid cells and the barely visible endothelial lining.

two fairly large, dense accumulations of lymphoid cells without germinating centers. Numerous small blood vessels were present in the wall.

High Power: Again the endothelial lining and the subendothelial delicate stroma, containing a number of blood vessels, accumulations of lymphoid cells and a few scattered epithelioid and large mononuclear cells, were observed.

Block IV, Section *a*: A section (×6¼) from this area (fig. 17) showed a small cyst at the margin of the hygroma and adjoining a mass of muscle fibers. The delicate fibrillar wall of the cyst may be seen in the upper part of figure 17. At the right border of the cyst, at *A* and *B*, a large area of hygromatous stroma penetrated, separating and destroying muscle fibers. Numerous dark-staining fibrillar serpentine streamers or sprouts, some of which are indicated by the

arrows, insinuated themselves between masses of muscle. They were derived from the lining wall of the cyst and, as shown in the illustration, coursed some distance into the muscle, finally to be lost in the peripheral zones. Within the circle *C* is seen a small cyst with dark granular contents which developed from a fibrillar membrane. Arising from its wall can be seen several serpentine cords, penetrating the surrounding muscle. In the circle *D*, an elongated, narrow slitlike cyst formed by canalization of a fibrillar cord. (The areas enclosed in circles *B*, *C* and *D* are shown in the higher powers in figures 18, 19, 20, 21 and 22.)

Block IV, Section *b*: The area enclosed in circle B in figure 17 was magnified 50 times (fig. 18). The muscle fibers immediately adjoining the cyst appeared as the merest atrophic filaments. The stroma of the hygromatous tumor penetrated a mass of muscle, with resultant isolation and destruction of muscle fibers. Farther away from the cyst, as seen in the lower portion of the photomicrograph, the

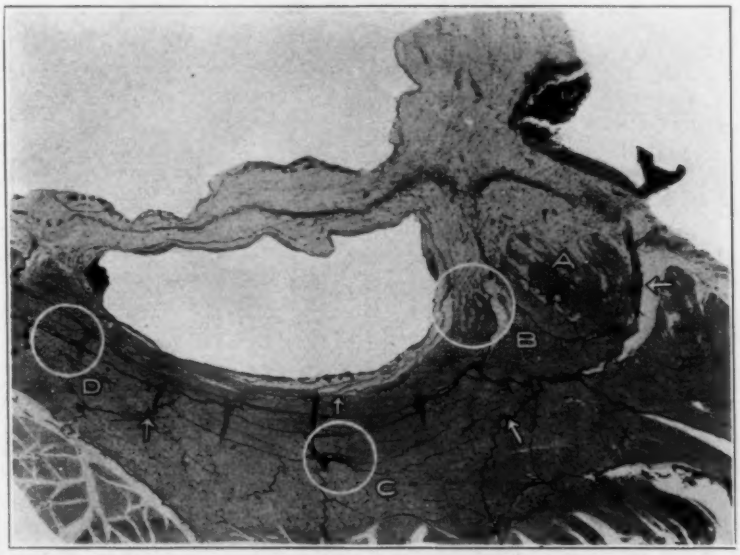

Fig. 17 (case 2).—A photomicrograph (× 6¼) of a section from area IV in figure 14 *A*. It illustrates the conditions found at the outer growing edges of a hygroma, which in this case is invading the deltoid muscle. Note the marginal cyst and the stroma of the tumor invading, separating and destroying the muscle fibers at *A* and *B*. Dark-stained serpentine sprouts or shoots of endothelial fibrillae, derived from the lining wall of the cyst and indicated by the arrows, are seen coursing between masses of muscle. In circle *C* a small cyst has been formed by the secretion between the fibrillae and the subsequent canalization of the sprout. (Higher power photomicrographs of these areas are shown in figures 18, 19, 20, 21 and 22.)

N. B.: The original magnification × 16 is reduced to × 6¼.

muscle appeared more normal. The cyst wall was very delicate, areolar in structure and composed of fine hyaline connective tissue. (Compare with fig. 18 *A*.)

Block IV, Section *c*: Another section from this area (fig. 19, × 100) showed hygromatous tissue penetrating several clefts between masses of striated muscle.

Fig. 18 (case 2).—A photomicrograph (× 50) of the area enclosed in the circle *B* in figure 17, illustrating some of the conditions found at the growing edge of a hygroma. Note the destruction of the muscle produced by the penetration of the tumor stroma between the muscle fibers.

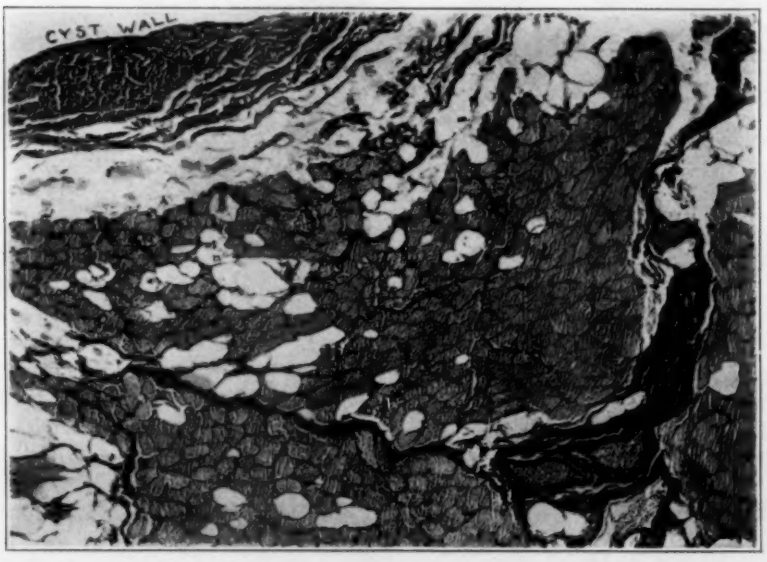

Fig. 18 *A* (case 2).—A photomicrograph (× 85) of a section from area IX, figure 14 *A*. The destructive action of the hygromatous stroma on an area of muscle is illustrated. Note the vacuolated appearance due to the disappearance of many of the muscle fibers and their replacement by fat, and the infiltrating fibrillar membranes.

A small newly formed cyst was present in the fibrillar cord, coursing through the center of the section. Minute cysts were seen elsewhere between the fibrillae. In the higher power magnification (fig. 20, × 350) the cyst was seen to contain lymph, in which there were large numbers of refractile bodies. The typical endothelial lining is well shown in the photomicrograph, as is the areolar stroma on the left. Striated muscle fibers, not yet injured by the growth of the cyst, are also apparent.

Block IV, Section *d*: Another section from this area (fig. 21, × 100) represented a mass of striated muscle bordering on a cyst. Throughout this mass of muscle tissue, fibrillar cords or streamers insinuated themselves between the muscle bundles and eventually divided to surround individual muscle fibers. In the

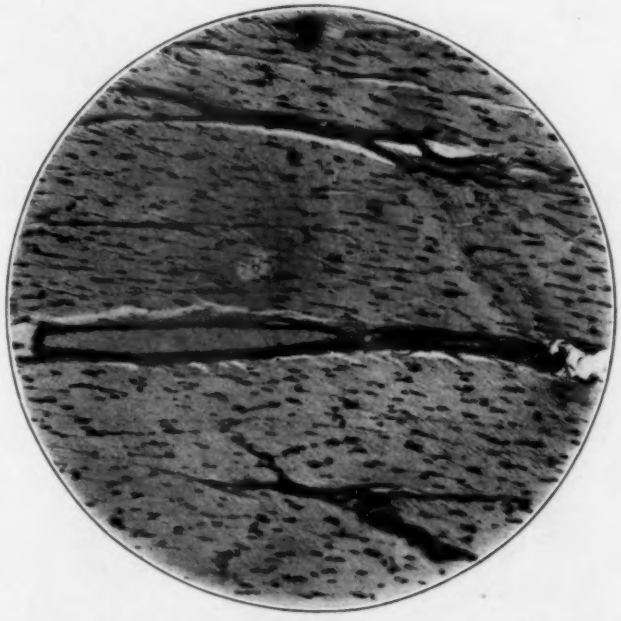

Fig. 19 (case 2).—A photomicrograph (× 100) of a section taken from area IV in figure 14 *A*, shown in low power in circle *D*, figure 17. Several fibrillar shoots of hygromatous stroma are seen penetrating clefts between bundles of muscle. A minute young cyst has been formed by the lymph secreted by the endothelial fibrillae of the shoot. New cysts are characteristically born by this process of secretion within and the subsequent canalization of the fibrillae.

center of the section, the endothelial fibrillae were separated by secretion and enclosed a newly formed cyst, containing pale-staining coagulated lymph, masses of degenerating nuclei, fragments of tissue and cellular débris. The cyst was lined by endothelium. To the right of the large cyst a smaller cyst was being formed.

Block IV, Section *e*: The higher power magnification (fig. 22, × 250) of the cyst shown in figure 21 showed its contents to be composed of lymph, in which were isolated groups of conglomerate nuclei, evidently the remains of disintegrated cells, and the remnants of degenerating muscle fibers. In the extremity of the

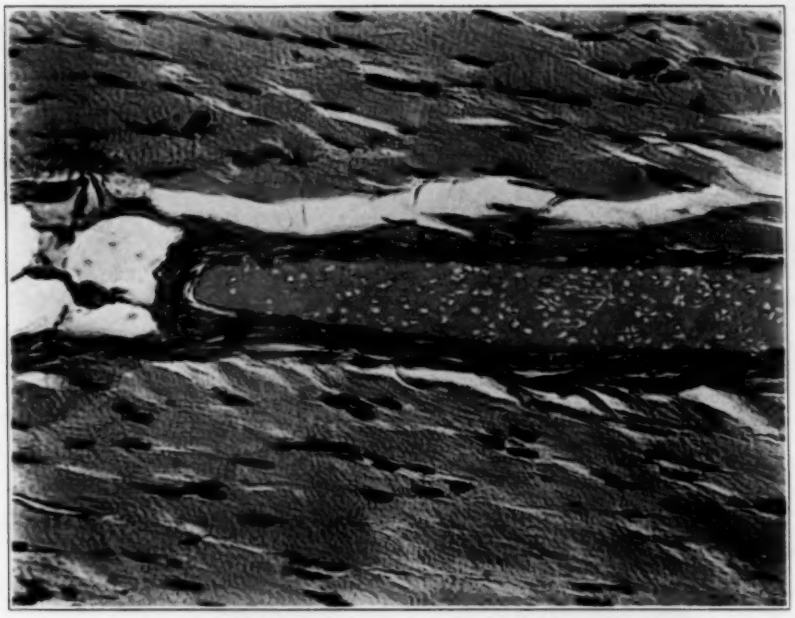

Fig. 20 (case 2).—A photomicrograph (× 350) of the cyst shown in figure 19. Note the endothelial lining and the spongy hygromatous stroma on the left, continuous with the endothelial fibrillar wall of the newly formed cyst. The adjacent muscle has not yet suffered from the growth and pressure of the cyst.

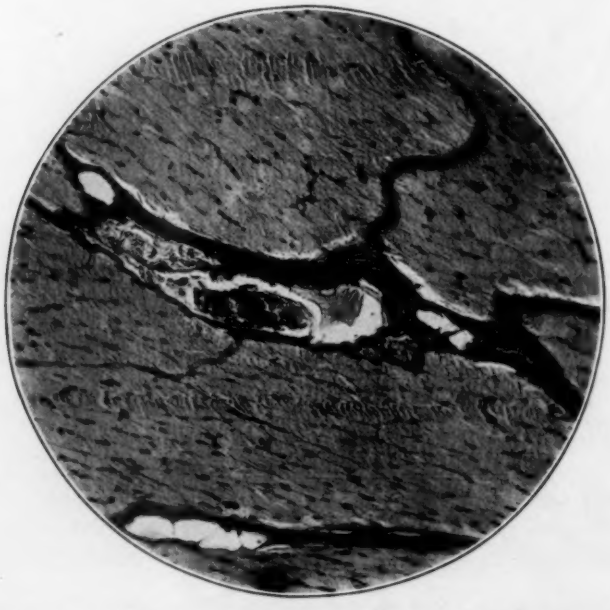

Fig. 21 (case 2).—A photomicrograph (× 100) of a section from area IV in figure 14 *A*. Endothelial fibrillar shoots are seen penetrating areas of muscle. In the center the fibrillae have been spread apart by secretion of lymph to form a new cyst, in which are seen remnants of tissue inclusions. Note the minute cysts at the extremities of the larger cyst.

cyst shown at the left of figure 22, a cross section of a nerve fiber enclosed in an endothelial cover can be recognized. The endothelial lining of the cyst is well shown.

Block V. Low Power: A section from this area, which included a cyst and the adjoining muscle, showed very well the isolation, degeneration and fragmentation of the individual fibers. This was especially well shown in the zone bordering directly on the cyst wall and in the area in which the hygromatous tissue was seen penetrating the muscle. The character of the hygromatous stroma was the same as has been previously described.

High Power: The section previously described in the low power view showed a longitudinal zone of hygromatous tissue running through the center and an oval, newly formed cyst, which had enclosed small segments of striated muscle fibers.

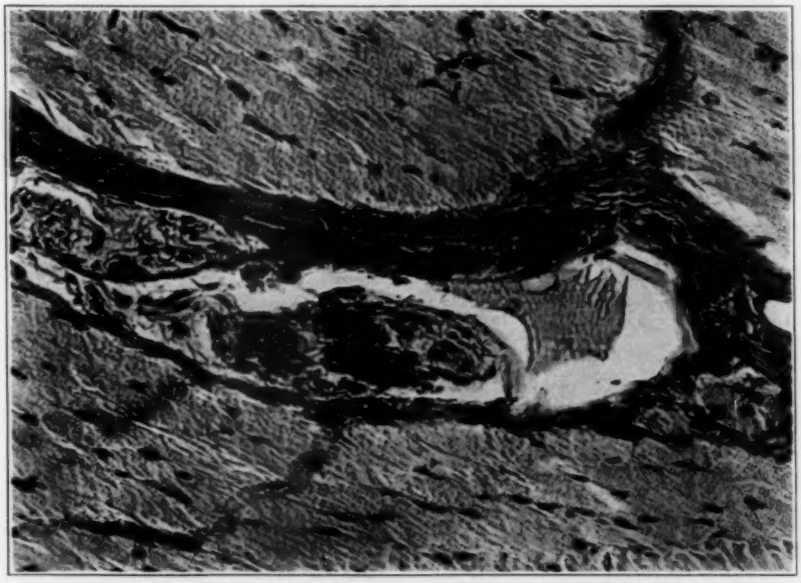

Fig. 22 (case 2).—A photomicrograph (× 250) of the cyst illustrated in figure 21. Note the cellular débris within the cyst and the mass of conglomerate nuclei, among which fragments of muscle fibers can be recognized. A nerve fiber enclosed in an endothelial envelop is seen on the left. Normal tissues are thus destroyed by a process of sequestration within the cysts.

They were isolated and disintegrating. In this small cyst a minute amount of definitely recognizable foamy secretion was seen, containing a number of small round and spindle-shaped cells. The wall of the cyst was composed of fine fibrillae and endothelial cells and was two or three cell layers thick. The hygromatous endothelial tissue was seen enclosing a nerve fiber cut in tangential section, and the endothelial shoot ran along as a delicate cord, in which newly formed capillaries and minute lymph spaces were seen, and which eventually disappeared in a few parallel fine fibrillae.

Block VI, Section *a*: In the lower half of the photomicrograph (fig. 23, × 100) illustrating this section is seen a large area of hygromatous tissue containing numerous blood vessels, lymph spaces, a cross section of nerve fiber, and near the

middle of the section an irregularly shaped cyst. In the upper half, a large area of striated muscle fibers is apparent. The cyst was newly formed, thin walled and lined with endothelium. It contained frothy, blue-staining, semihomogeneous, coagulated lymph. Isolated and free in this lymph (enclosed in the circle in figure 23) were a number of fragments of striated muscle fibers. In the left half of the cyst are seen groups of conglomerate poorly stained nuclei, with small amounts of protoplasm, several large mononuclear cells, a few lymphoid cells and cellular débris. (These nuclei and cellular remnants were evidently the remains of degenerated tissue cells.)

Block VI, Section *b:* The photomicrograph in figure 24 shows the fragments of muscle fibers indicated within the circle in figure 23 to be poorly stained,

Fig. 23 (case 2).—A photomicrograph (× 100) of a section from area IV, figure 14 *A*, illustrating a cyst in hygromatous stroma adjacent to a mass of deltoid muscle. Note the isolated fragments of muscle shown within the circle and the remains of degenerated cells and nuclei to the left. Note the vascularity of the tumor stroma.

hydropic, shriveled and atrophic, with barely visible striations. The nuclei were swollen. In areas the muscle fibers were undergoing solution. In the cystic fluid around the fragments were a number of lymphoid and epithelioid cells.

Block VI, Section *c*: A section (fig. 25, × 100) showed masses of muscle fibers between which was hygromatous stroma. Incorporated in one muscle bundle was a thin-walled, irregularly shaped cyst. The muscle fibers immediately around the cyst were atrophic and frayed out. Enclosed within the cyst were isolated fragments of longitudinally sectioned light-staining muscle fibers.

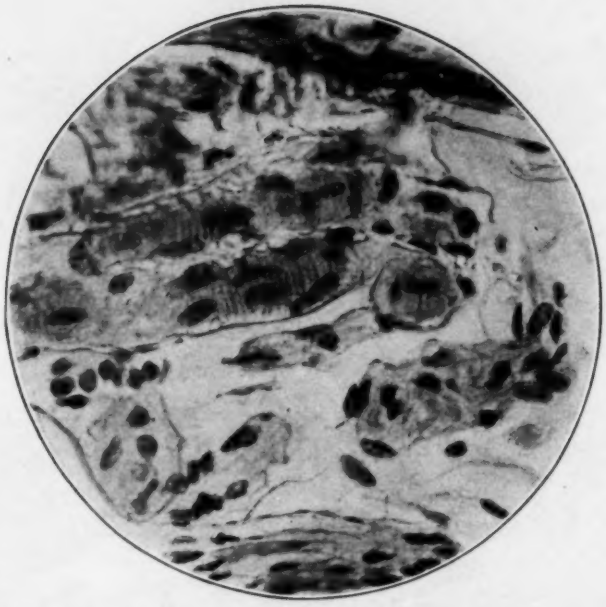

Fig. 24 (case 2).—A photomicrograph (× 500) of the fragments of striated muscle fibers isolated in the cyst, shown within the circle in figure 23. The fibers have undergone almost complete solution. Hydropic degeneration, disintegration and almost complete loss of striations are apparent.

Fig. 25 (case 2).—A photomicrograph (× 100) of a section from area VI, figure 14 *A*. A cyst has formed in the tumor stroma which has infiltrated the muscle. Sequestrated within the cyst are a number of muscle fibers. The fibrillar stroma and the injury to the muscle around the cyst are readily seen.

Block VI, Section *d:* The cyst in the section described in the previous paragraph was seen in the higher power magnifications (fig. 26, × 250) to contain numerous striated muscle fibers in longitudinal section. Some of the fibers were lightly stained, had lost their striations and were undergoing a beginning hydropic degeneration. Endothelial cells were penetrating between the fibers. There were areas in which the fibers had undergone almost complete solution and were recognized as masses of granular débris. The endothelial lining and the fibrillar connective tissue in the wall of the cyst are well shown in figure 26.

Block VII: A section from area VII, figure 14 *A*, showed another area of muscle adjoining a cyst. Hygromatous tissue was seen penetrating the muscle and causing isolation, atrophy and fragmentation of the muscle fibers. Between the muscle fibers were seen endothelial and large mononuclear cells.

Fig. 26 (case 2).—A photomicrograph (× 250) of the cyst shown in figure 25. The details are here more apparent. The muscle fibers engulfed within the cyst are largely undergoing degeneration and fragmentation. In several, however, the striations are still preserved, indicating that the cyst is young and that the sequestration of these muscle fibers is a fairly recent event. The general character of the tumor stroma about the cyst is well illustrated.

Block VI, Section *e*: In section from area VI in figure 14 *A* (fig. 27, × 150) a mass of deltoid muscle fibers was in close proximity to the growing edge of the hygroma. There was some endothelial invasion between the muscle fibers, which showed transverse fragmentation, atrophy, poor affinity for stain, irregularity of caliber and almost complete disappearance of the striations. (This is a characteristic finding in voluntary muscle undergoing injury, as has been noted in a muscle infected with Trichina.)

Block VI, Section *f:* A mass of muscle fibers adjoining a cyst showed the separation and atrophy of the fibers produced by the penetration of hygromatous stroma (fig. 28, × 100). In the center of the photomicrograph one sees a small

Fig. 27 (case 2).—A photomicrograph (× 150) of a section from area VI, figure 14 *A*, showing a mass of muscle fibers (deltoid) at the growing edge of the hygroma. Note the atrophy and numerous transverse fractures of the individual fibers, which have been weakened by the growth of the tumor. The penetration of hygromatous stroma between the fibers is illustrated in the upper half of the section.

Fig. 28 (case 2).—A photomicrograph (× 100) of a section from area VI, figure 14 *A* in immediate proximity to the hygroma, showing the zone of infiltration of tumor stroma between the muscle fibers. The main growth is toward the left of the muscle shown in this section. Note the atrophy with tapering and complete disappearance of the muscle fibers. Attention is directed to a small bundle of fibers in the center of which two segments of a fractured fiber are seen.

bundle of muscle fibers surrounding a small cyst and several fragments of hydropic degenerating muscle fiber. Figure 29 (× 350) represents the same section as that shown in figure 28. One sees two fairly normal-looking striated muscle fibers separating to enclose a small cyst; a fragment of swollen, hydropic muscle fiber showing a loss of striations, and swollen fibrillae. The cyst and the fragments of muscle were surrounded by a fine membrane containing nuclei of the endothelial type.

Block IV, Section *a*: Van Gieson's stain showed a large area of dense muscle infiltrated with hygromatous fibrillar membranes (fig. 30, × 85). The latter stained a rich red, which sharply differentiated them from the surrounding muscle (yellow). A small cyst was formed within one of the fibrillar membranes and contained small fragments of muscle.

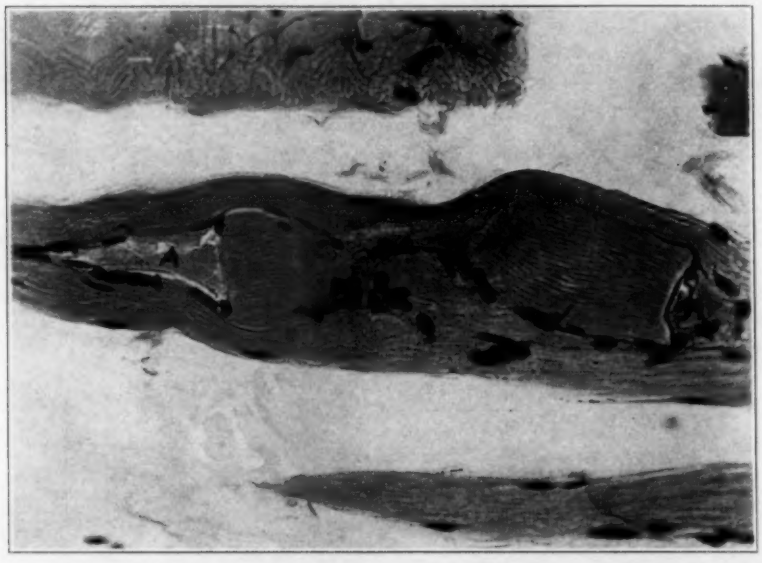

Fig. 29 (case 2).—A photomicrograph (× 350) of the muscle bundle enclosed in the circle in figure 28, consisting of two segments of muscle fiber confined within two fairly normal appearing fibers, the striations of which are barely visible. The segments of fractured fibers show hydropic degeneration and have lost their striations. Note the newly formed cyst, *A*, at the end of each segment.

Block IX, Section *a*: In figure 31 (× 200) dense zones of fibrillar stroma are seen between bundles of muscle. In the lower portion of the field (*A*) large globules of fat are seen in the membranes. This fat resulted from fatty degeneration of muscle fibers.

Block IX, Section *b*: In the lower portion of the field (*A*, fig. 32) the osmic acid stain showed rows of fat globules in the central axis of the muscle fibers. In the upper part of the field (*B*) these fatty fibers coalesced to form large areas of adipose tissue.

Case 3.—J. P., a white boy aged 6 months, was admitted to the Long Island College Hospital on March 15, 1927, because of a tumor on his right shoulder since birth. He died March 18.

Fig. 30. (case 2).—A photomicrograph (× 85) of a section from area IV, figure 14 *A* (Van Gieson's stain), representing a large area of dense muscle. Observe the marked infiltration of the hygromatous fibrillar membranes between muscle fibers and the small cyst to the right which has formed within the fibrillae and which contains small fragments of muscle.

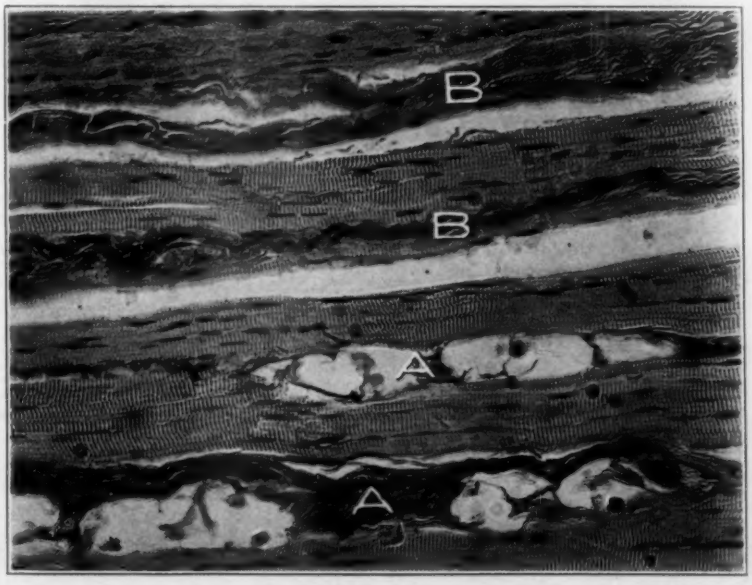

Fig. 31 (case 2).—A photomicrograph (× 200) of a section from area IX, figure 14 *A*, illustrating the penetration of hygromatous stroma, *A* and *B*, into the clefts between bundles of muscle fibers. The stroma in the lower field, *A-A*, is seen to contain large globules of fat resulting from the fatty degeneration of muscle fibers previously enveloped and destroyed by the hygromatous sprouts. In the upper field, *B-B*, two fibrillar membranes are depicted. Notice the fibrillar character of the infiltrating membranes.

History.—There was no history of syphilis or tuberculosis. The birth was normal, the child weighing between 7 and 8 pounds (3,175.14-3,628.73 Gm.). He was breast fed, and his general health and appetite had been good. He had been gaining an average of 7 ounces (198 Gm.) per week. The tumor, which was noticed at birth, extended from the right ear over the shoulder and posteriorly over the back (fig. 33). It was somewhat larger than a grapefruit. The mother thought the mass increased in size when the child cried. The tumor had been aspirated when the child was 2 months old. It was reduced in size, but had since grown constantly larger. There were no symptoms. A clinical diagnosis of branchial cyst was made previous to the patient's admission.

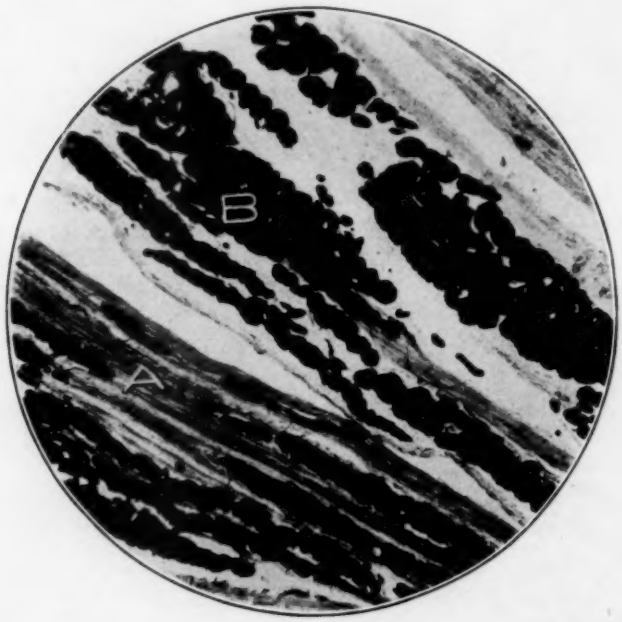

Fig. 32 (case 2).—A photomicrograph (× 45) of a section from area IX, figure 14 *A* (osmic acid stain), showing an area of compressed muscle, which adjoined a marginal cyst. Attention is directed to the longitudinally sectioned muscle fibers. In the central axis of several of these fibers, *A*, rows of fat globules are seen—an early stage of fatty degeneration. With further degeneration of muscle, these fat globules increase in number and size and replace entirely the muscle fibers. These fatty fibers, now transformed into fat, coalesce to form large areas of adipose tissue, *B*.

Examination.—The general examination gave negative results except with reference to the tumor. On the right side of the neck, extending from the ear, the ramus of the jaw and the midline across the shoulder and downward over the back and scapula, was a multilobulated cystic tumor which was sessile and could be shifted about to some extent. It was soft, fluctuant and nowhere red or tender. Certain of the lobulations of the tumor were definitely fluctuant and fluid containing, while others were firm and nodular. The overlying skin was thin and atrophic. The size of the mass caused the head to be carried well toward the left. The mass

measured 20 cm. in vertical diameter and about 18 cm. in transverse diameter. The movements of the right arm and shoulder were approximately normal.

The temperature was 97.6 to 99.8 F., the pulse rate 110 and the respiratory rate 28. The erythrocyte count was 4,800,000, the hemoglobin content 67 per cent and the leukocyte count 8,400. There were 24 per cent polymorphonuclears, 74 per cent small and large mononuclears and 2 per cent transitional cells. The examination of the urine and the Wassermann test gave negative results. There was a preoperative diagnosis of hygroma.

Operation.—The hygromatous tumor was excised on March 18, with the patient under ether anesthesia. The dissection was begun by outlining a lenticular area of skin over the large, multilobular cystic mass on the right side of the neck. The dissection was continued on the lateral and posterior aspects, whereupon the tumor was found to extend beneath the trapezius muscle, a considerable portion of which had to be sacrificed. Anteriorly, further operation exposed the supraclavicular fossa, the jugular vein and bulb, the carotid artery, the vagus nerve and finally the phrenic nerve. The tumor was then followed posteriorly in order to remove the

Fig. 33 (case 3).—A cystic hygroma in a boy 6 months of age. The tumor was present at birth and grew progressively larger. It was lobulated and fluctuant in certain areas and firm and nodular in others. The mass measured 20 cm. by 18 cm. The operation required for the excision of the tumor was very extensive, and the child succumbed some hours later. This was the only fatality in the series.

extensive subscapular portion. By sharp dissection the entire mass was then liberated from the ribs and the lateral aspect of the neck, to both of which it was in many areas densely adherent. At the moment of dissection along the great vessels and the vagus nerve, the patient showed marked signs of shock and the general condition was poor. After the administration of saline solution there was some improvement. Thereupon, a prolongation of the general tumor mass was found to extend anteriorly almost to the thyroid gland and the larynx, where it ended blindly. A communication between the cystic tumor and the venous circulation could not be definitely demonstrated. The wound was closed in layers, and drains were placed. The child's condition was only fair at the end. The operative procedure consumed about one hour.

Postoperative Course.—Evidences of shock continued after the close of the operation. A transfusion of 35 cc. of blood was given together with saline infusion

and epinephrine. Dextrose solution was administered by rectum. All supportive measures failed, and the child died at 6:45 p. m. on the day of operation, as a result of shock and cardiac failure.

Gross Pathologic Examination.—The specimen, a tumor of the neck, measured 17 by 11 by 7 cm. (fig. 34). It was composed of a conglomeration of cysts varying from 0.5 to 6 cm. or more in diameter. The cysts were mostly thin walled; in certain areas they were transparent and in other areas they contained a considerable amount of white fibrous tissue. The inner lining of the cyst was smooth and glistening. The cyst contents were seen to be a clear straw-colored fluid, and a few of the smaller cysts contained some blood. They were bound together by a considerable mass of fibrous tissue, in which were seen large blood vessels. In

Fig. 34 (case 3).—A photograph of the gross specimen removed from the patient shown in figure 33. The mass was multilocular and composed of thin-walled cysts of varying sizes. There were firm areas in which there was abundant fibrous tissue. The fluid within the larger cysts was clear and straw colored, while several of the smaller cysts contained blood. The specimen measured 17 by 11 by 7 cm. One of the larger cysts has been opened, and the glistening wall shows trabeculation and numerous recesses.

one area was found a group of enlarged lymph glands, which on gross examination appeared normal.

Microscopic Examination.—The tissue showed enormously dilated lymph spaces of irregular outline and large dilated blood vessels. The cysts were lined by endothelium, and in the stroma surrounding the cysts were large accumulations of lymphoid cells. Heavy fibrous trabeculae were also seen. The appearance in general was much like that in the cases previously described (cases 1 and 2).

Low Power: A longitudinal section of lymph gland 1.4 cm. in diameter was examined. The most striking feature was the frequent occurrence of large and small lymphoid follicles in the cortical zone of the gland, which was thick. Numerous small follicles were seen in the deeper portions of the cortex. In the hilus were seen large lymph spaces, in some of which occurred large numbers of lymphocytes and here and there small follicles.

High Power: The germinating centers were large and hyperplastic in appearance, containing the large lymphoblastic cells in addition to the prelymphocytes. A thick cortical zone of lymphoid cells was seen around each germinating center. Further details resemble those of the lymph glands described in case 1 (figs. 11 and 12). The lymph gland was definitely hyperplastic. The diagnosis was hygroma with hyperplastic lymph gland.

CASE 4.—C. L., a Negro girl aged 16, was admitted to the Long Island College Hospital on June 16, 1927, because of a swelling with periodic discharge on the neck and beneath the tongue on the left side (fig. 35). She was discharged July 2.

Family History.—Both the father and the mother had died of pulmonary tuberculosis.

History.—The patient's general health had always been good prior to the onset of the complaint. There had been frequent severe headaches and dizziness since the appearance of the swelling, three years before. There was a constant sensation of a lump or swelling in the throat on the left side, but there had been no difficulty in swallowing or breathing. There had been no loss of weight. The onset of menses occurred at the age of 12; the periods were always regular. The patient had been married eleven months and had one child.

Three years before, the patient became aware of a swelling located under the left side of the tongue and extending into the submaxillary area. After the first appearance of the swelling, incision and drainage were necessary to relieve pressure. These incisions were made externally over the greatest prominence. There was a temporary diminution in size, followed by a rapid reappearance of the swelling which would discharge spontaneously, often at intervals of three to four days. A year and a half after its first appearance, the tumor had extended downward into the upper part of the anterior triangle. Both internal and external incisions were made at that time. After temporary diminution in size, the swelling reappeared and fluctuated in size from that of a lime to that of an orange. After incision intraorally, a year and a half before, there had been no further sublingual swelling until the preceding week, when the swelling under the tongue again appeared, discharged three days later and then apparently disappeared.

Examination.—The patient was a married Puerto Rican woman, aged 16. Her teeth were in poor condition. A depressed scar was seen in the floor of the mouth on the left side. Examination of the throat gave negative results. There was a swelling on the left side of the neck, occupying the region of the upper anterior triangle and extending from the angle of the jaw, through the submaxillary and submental areas, well beyond the midline toward the right. An oval, elongated tumor the size of an egg extended downward to the lower border of the thyroid cartilage. A large, wide, irregular, horizontal, keloid scar crossed over the prominence of the mass. The swelling was not definitely fluctuant, indurated or tender, and no masses were felt within its evidently fluid contents. The overlying skin, except in the area of the scar, was not adherent. The associated cervical glands were not enlarged. The thyroid gland was distinctly separate from the swelling and could be readily palpated. It was moderately enlarged and showed no abnormalities.

The systolic blood pressure was 108 and the diastolic 68. The erythrocyte count was 3,650,000, the hemoglobin content 78 per cent and the leukocyte count 15,200. There were 56 per cent polymorphonuclears, 32 per cent small mononuclears, 11 per cent large mononuclears and 1 per cent transitional cells. The examination of the urine gave negative results.

Operation (Dr. E. J. Browder).—The hygroma of the left submaxillary region was excised on June 20, with the patient under nitrous oxide and ether anesthesia. The old scar was excised, and the incision was extended downward along the anterior border of the left sternocleidomastoid muscle. It was soon evident that the swelling was a typical cystic hygroma which occupied the entire submandibular area, extended medially well beyond the submental area and the midline, occupied the entire left anterior triangle and extended downward to the episternal notch. Dissection was begun from the lateral aspects. The swelling was firmly adherent to the sternocleidomastoid muscle, a portion of which had to be excised in order to

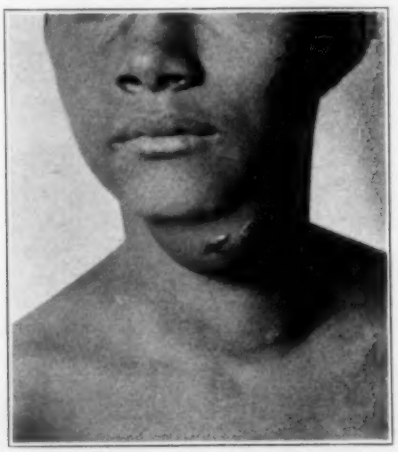

Fig. 35 (case 4).—A hygromatous tumor in a Negro girl, aged 16. The mass appeared three years previously. Several incisions had been made externally and intraorally, followed by infection and prolonged drainage. The tumor reappeared after each incision. The hygroma involved the left submaxillary triangle, the floor of the mouth and the under surface of the tongue. The growth was far more extensive than one would anticipate from the apparent size before operation. It was unilocular and contained a thick mucoid material, probably the result of previous infection.

be certain of removing the outer limits of the tumor. Medially, the mass was seen to be lying directly on the left lobe of the thyroid gland. The sternohyoid muscle was divided in order to liberate the extension of the tumor medially. A wide dissection had to be carried out in order to circumscribe the extensions of the tumor growth. Thus it was found necessary to remove the submaxillary gland together with a considerable number of enlarged adjoining lymph nodes, which were not only firmly adherent to the tumor mass but in several instances incorporated in it. The lower limits of the tumor reached almost to the episternal notch. The swelling was far more extensive than it was thought to be from the apparent size before operation. No definite pedicle connecting with the jugular vein was found. The

entire mass was finally removed in toto. The thyroid gland, which was of colloid appearance and considerably larger than normal, was exposed in the dissection. Fine interrupted silk sutures were used for the subcutaneous tissues and the skin. One small drain was placed.

Postoperative Course.— June 21: When a drain was removed, there was an escape of a small amount of mucilaginous material, resembling in appearance and consistency that which was seen and removed at the time of operation.

July 2: A small fluctuant area in the wound was opened, and 10 to 15 cc. of a thin yellowish mucoid substance was evacuated. The patient was discharged. The wound was healed except at the point of the former drain. There was a small amount of tenacious, yellowish liquid drainage.

Gross Pathologic Examination.—The specimen, a tumor of the neck, was a sausage-shaped unilocular cyst 10 cm. long and 4 cm. in diameter, containing a thick, glairy myxomatous material resembling Wharton's jelly. The wall of the cyst was extremely thin, and the inner surface, was smooth and glistening. At one end the cyst was firmly attached to the salivary gland. Around the cyst proper there was a wall of thick fibrous tissue.

Microscopic Examination.—The wall of the cyst was composed of dense fibrous tissue, containing large numbers of lymphoid cells. The cyst was lined with a poorly formed granulation tissue showing evidence of old infection. The diagnosis was hygroma.

Follow-Up Note.—No answer to the questionnaire was received. The patient could not be traced.

Case 5.—E. P., a white woman aged 34, was referred to the Long Island College Hospital by Dr. Henry Mills with the diagnosis of "deep cervical cyst" and admitted on Oct. 9, 1922, because of a fluctuating swelling on the left side of her neck and "nervousness." She was discharged October 18.

History.—The patient was the fourth of seven children. Her general health had been good. The menses were normal. A swelling had appeared under the left jaw about twenty years before and later disappeared. A recurrent swelling had been noticed ten years before. Except for slight nervousness, there were no complaints except those referable to the swelling on the left side of the neck. The present enlargement had appeared rather suddenly four months before and recently had become larger (fig. 36). There was a history of fluctuation in size. There had been no preceding infection of the ears, nose, tonsils or throat. She felt a stiffness in her neck when she turned her head. There had been no dysphagia, dyspnea or pain. There were no symptoms referable to her left arm. She had been feeling very well. Ferrous iodide was prescribed under the assumption that the tumor might be a goiter.

Examination.—The patient was well nourished and apparently in good health. She weighed 129 pounds (58.5 Kg.). The patient held her head and neck flexed slightly to the right. Under the left sternocleidomastoid muscle there was a large oval swelling which extended into the posterior triangle and anteriorly to the midline. As she swallowed, there was very little movement of the mass, which seemed not to be connected with the trachea or thyroid gland. There was no visible throbbing in it. The mass was smooth, fluctuant and not tender. In it were semisolid areas but no nodules. It extended from the mastoid process to the angle of the jaw and continued anteriorly under the ramus of the mandible almost to the midline and downward to the clavicle and the left sternoclavicular joint. The larynx and trachea were displaced to the right. The thyroid gland was barely palpable. Thrills or bruits were not demonstrable in the tumor. There

was no enlargement of the lymphatic glands on either side of the neck. The tumor measured 10 cm. in transverse diameter and 12 cm. in vertical diameter. There was no retromanubrial dulness, nor was there any dulness over the pulmonary apexes. Examination of the heart, lungs, abdomen and extremities gave negative results. The pulse rate was 92 and regular. The radial pulse on the left was of good volume. The grip in the left hand was strong.

The erythrocyte and the differential count were within normal limits. The hemoglobin content was 90 per cent and the leukocyte count 1,300. The examination of the urine gave negative results. The preoperative diagnosis was cyst of the neck, of obscure origin and of benign nature, possibly of lymphatic or branchial cleft origin.

Operation.—On October 11, the hygromatous cyst of the left side of the neck was excised with the patient under nitrous oxide and ether anesthesia. A linear incision was made along the anterior border of the left sternocleidomastoid muscle from the angle of the jaw to the sternoclavicular joint. The anterior border of the muscle was dissected free and retracted. This procedure brought into view a bluish cyst with thin membranous semitransparent walls resembling serous

Fig. 36 (case 5).—An extensive cystic hygroma of the left anterior and posterior cervical triangles in a woman aged 34. There was a history of appearance of the swelling followed by disappearance over long intervals. The recent swelling was noted only four months previous to examination and had grown rapidly in size. There were no symptoms except a feeling of stiffness on movements of the head and neck. The mass extended from the mastoid process to the angle of the jaw, forward along the ramus of the jaw almost to the midline and downward to the left clavicle and the left sternoclavicular joint. The larynx and trachea were displaced to the right.

membranes. By careful division of dense connective tissue adhesions and by digital separation, delivery was made of the broad lower pole, which was hanging fairly free in the upper mediastinum. Anteriorly and medially the carotid artery and internal jugular vein were separated from the tumor. Dense adhesions were encountered under the sternocleidomastoid muscle and in the posterior triangle. The upper pole of the tumor was adherent and in intimate relation with several lymph glands situated below and anterior to the mastoid process. A small amount of watery fluid escaped from a perforation in the thin cyst wall. The upper pole with the adjacent lymph glands was then dissected free. After removal of the cystic mass, the upper and lower limits of the resulting cavity were touched with iodine to stimulate adhesions, with consequent obliteration. The cystic multilocular tumor contained a clear straw-colored fluid, on the surface of which cholesterol crystals could be seen. It appeared to be of lymphatic nature, and the

diagnosis of hygroma was made. There was a minimum of bleeding and no damage to important structures. The wound was closed in layers without drainage.

Postoperative Course.—October 18: The patient was discharged in good condition seven days after the operation.

Gross Pathologic Examination.—The specimen was a multilocular cyst. The walls of the cyst varied in thickness. In certain areas the membranous walls were extremely thin and transparent, while in other areas they were composed of broad bands of fibrous tissue.

Microscopic Examination.—There were small groups of lymphoid cells scattered through the walls. In some areas, there were structures resembling lymph nodes. The capillaries in the walls were congested. A large artery seen in the section showed marked arteriosclerosis. The lining of the cysts had the appearance of endothelium. A diagnosis of hygroma was made.

Follow-Up Notes.—Oct. 31, 1922: The patient made a return visit, twenty days after the operation. A well healed operative scar was seen. The neck was symmetrical and normal in appearance. There was a slight numbness over the upper part of the left side of the neck and along the lower ramus of the mandible. The movements of the left arm were entirely normal.

May 3, 1933: The patient was well, and there had been no symptoms referable to the operation or to the left arm. There was a fine linear scar along the anterior border of the sternocleidomastoid muscle. Sensation just under the front of the scar and along the ramus of the mandible seemed to be abnormally acute. There was no numbness. The movements of the head were unrestricted. The heart sounded clear. The pulse rate was 96 and the weight 156 pounds (70.8 Kg.). The left sternocleidomastoid muscle was possibly not quite as strong as the right. The movements of the face and mouth were normal. The patient stated that after removal of the tumor she felt a great relief and a feeling of freedom, and a "clearness" in the throat. She had not realized that swallowing, breathing and speaking had been somewhat interfered with. At the time of this examination, voice and respirations were clear and free.

There had been no recurrence ten and one-half years after operation.

Case 6.—W. R., a white boy, aged 13 months, was admitted to the Long Island College Hospital on Feb. 11, 1931, because of a cystic tumor under the right axilla since birth. He was discharged on March 8.

History.—The patient had had good health since birth. He was breast fed for two weeks, and then a formula was prescribed. The swelling on the right wall of the chest and in the lower part of the axilla had been present since birth, when it was the size of a half grapefruit. It had slowly enlarged with the growth of the child but had never caused any trouble. Redness or tenderness had not been noted. At the time of the patient's admission the tumor was the size of a large grapefruit (fig. 37).

Examination.—The patient was a well developed white boy 13 months old. Dental development was normal. Examination of the throat gave negative results except for markedly enlarged tonsils. The skeletal development of the thorax was symmetrical, and the respiratory movements were equal on the two sides. A large cystic swelling, fluctuant, soft and nowhere tender, extended from the right axilla over the whole right thoracic wall. It was attached to the deep structures and to the skin and was circumscribed but not sharply demarcated. The tumor transmitted light readily. It measured 5 by 5 by 4 inches (12.7 by 12.7 by 10.16 cm.). It had a wide sessile base. The general physical examination gave negative results.

The temperature was 99 F. The erythrocyte count was 4,250,000, the hemoglobin content 85 per cent and the leukocyte count 7,200. There were 63 per cent polymorphonuclears and 36 per cent small and large mononuclears. The examination of the urine gave negative results. A preoperative diagnosis of cystic hygroma of the right wall of the chest was made.

Operation (Dr. Francis Clark).—The operation was performed on February 18, with the patient under ether anesthesia. The incision was begun just below the clavicle at the junction of its middle and outer thirds and was extended obliquely downward and laterally to about the costovertebral angle. In several places the cystic lobulated tumor was intimately adherent to the skin and was opened in making the skin incision. A clear fluid escaped. The mass was separated from the skin and the subcutaneous tissue by sharp and blunt dissection. Before the mass could be completely liberated an extensive dissection had to be carried

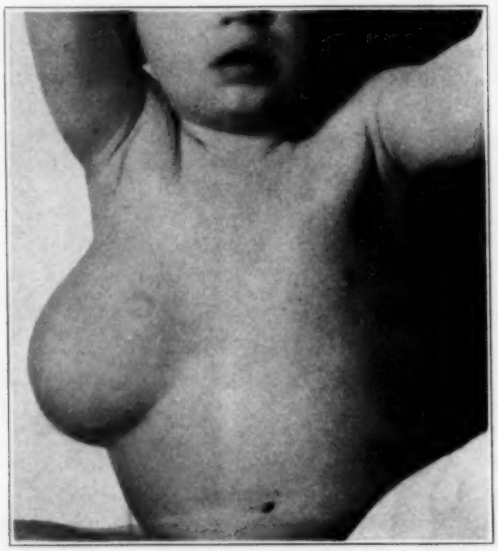

Fig. 37 (case 6).—A cystic hygroma of the right axilla and chest wall in a boy aged 13 months. The tumor was noticed at birth. It grew progressively larger but never caused any symptoms. The tumor was soft and fluctuant, transilluminated readily, measured 5 by 5 by 4 inches (12.5 by 12.5 by 10 cm.) and at operation was found to cover the anterolateral chest wall from the clavicle to the costal margin.

out, as the tumor was large and adherent to the anterior and lateral walls of the chest from the clavicle to the costal margin. No definite connection could be established between the upper extremity of the mass and the junction of the jugular and subclavian veins. The wound was closed and one drain placed under the skin flaps.

Postoperative Course.—There was no unusual postoperative reaction. A considerable amount of blood-stained serum drained from the wound. The sutures were removed on the seventh postoperative day. The wound healed well, and the child was in good condition one week after operation. He was discharged on March 7, 1931, seventeen days after operation.

Gross Pathologic Examination.—The specimen, a tumor of the right wall of the chest, had been excised with a large area of overlying skin, subcutaneous tissue and muscle. The cystic tumor was multilocular. The wall was smooth and of irregular thickness. Fluid contents had been lost.

Microscopic Examination.—One large representative block of tissue was preserved for microscopic examination.

Low Power: The greater part of the section comprised a collapsed cystic cavity, the walls of which were immensely thickened and composed of a hyaline fibrillar connective tissue.

High Power: In certain areas between the connective tissue fibers there was a foamy blue-staining material contained in small spaces and possibly representing coagulated secretion. This had been seen in some previous instances. This blue-stained material contrasted readily with the more pink-staining fibers themselves. Projecting into the main cystic space and dividing it into irregular compartments, was a folded bar or trabecula of great delicacy. It was lined by the typical endothelial layer, below which was a fairly dense, pink-staining connective tissue, which was moderately cellular. Running through the center of the bar in the nature of a core, there was a zone of extremely fine areolar, reticular, clear, loose connective tissue. This gave to the central zone of the wall an almost transparent appearance. Small blood vessels were numerous. There were a few aggregations of lymphoid cells and the earliest beginnings of follicles were seen. These accumulations of lymphoid cells were occasionally seen immediately below the endothelium. In these areas were also lymphoblastic cells, such as are seen in the early germinating centers. These were evidently the beginnings of newly formed lymphoid follicles. The stroma outside of this large cyst showed the general structure of the ground substance previously described, namely loose, areolar, reticular, almost transparent tissue, in which occurred large numbers of small cyst spaces, small blood vessels, nerve fibrils and loose, meshy, endothelial fibrillar substance, forming new lymph spaces. The diagnosis was hygroma.

Follow-Up Note.—May 6, 1933: No answer to the questionnaire was received. The patient could not be traced.

CASE 7.—L. W., an obese woman aged 38, weighing 197½ pounds (89.6 Kg.), was admitted to the Long Island College Hospital June 19, 1930, complaining of a lump on the right side of the neck of six weeks' duration, a pain in the back of the neck radiating to right ear and stiffness of the neck. She was discharged June 25.

History.—The patient had been married thirteen years. There had been three pregnancies. Her general health had been good. She had been obese for several years. Her greatest weight was 200 pounds (90.7 Kg.). For the past year, on awakening in the mornings she had noticed a stiffness of the neck, which "limbered up" during the course of the day. At first she felt a heaviness and fatigue referred to the neck, and more recently she complained of pain on the right side of the neck which radiated to the right ear and which was increased by bending of the head and neck to the right. She stated also that the right arm became easily fatigued, and occasionally she noticed discomfort and a feeling of numbness in it. Six weeks before her admission a mass had been noticed on the right posterior aspect of the neck. There had been no noticeable increase in the size of the swelling.

Examination.—The general examination gave negative results except with reference to the enlargement on the right side of the neck and the cardiac findings. The neck was short, broad and heavy. There was a rounded, globular prominence

about the size of a tangerine under the lower third of the sternocleidomastoid muscle. It projected into the posterior part of the supraclavicular triangle and extended from the origin of the sternocleidomastoid muscle outward to the outer third of the clavicle and posteriorly to the border of the trapezius muscle. The mass was definitely circumscribed, fluctuant and not tender and had a somewhat lobulated structure. It was not attached to the skin and was loosely attached to the deeper structures. The cervical lymph nodes were not enlarged. There was no retromanubrial dulness. The examination of the heart showed numerous extrasystoles, and an electrocardiogram showed a perfect trigeminal rhythm. The auriculoventricular conduction time was normal. There were no abnormalities indicative of ventricular myocardial disease. No definite sensory changes were found in the right arm, but the grip of the right hand was not as strong as that of the left.

The clinical examination gave negative results with reference to pulse, temperature, urine and blood. The preoperative diagnosis was lipomatous tumor on the right side of the neck extending under the sternocleidomastoid muscle and projecting into the posterior triangle. The pain radiating to the back of the head and neck and to the right ear and the discomfort and numbness of the right arm were believed to be due to pressure on the nerves of the cervical and brachial plexuses.

Operation.—The hygroma was excised on June 20, with the patient under nitrous oxide and ether anesthesia. An incision was made horizontally across the posterior triangle starting at a point about 1½ inches (3.8 cm.) above the origin of the sternocleidomastoid muscle, and ending at the anterior border of the trapezius muscle. Very soon there appeared a tumor presenting a bluish reflex and the thin transparent walls characteristic of a hygroma. The fluid within was of a thin, watery, straw-colored, lymphlike character. Digital dissection was largely employed. The greater part of the tumor was liberated without difficulty. The anterior jugular vein, which was adherent to the anterior margin of the tumor, was separated from it and retracted medially. The mass was the size of a lemon and was attached by a number of strands at the junction of the internal jugular and subclavian veins. Otherwise the tumor was relatively free. No free communication with the subclavian vein could be demonstrated. The tumor was thereupon extirpated in toto. A small gauze pack was placed in the remaining cavity and the wound closed in layers with fine silk.

Note: The tumor consisted of one large cystic compartment and a number of smaller loculations. The posterior border of the tumor had been covered with a large pad of fat, characteristic of obese persons. It was this fat deposit which caused the lobulated feel and thus led to the tentative, preoperative diagnosis of lipoma. The tumor had rested directly on the cords of the brachial plexus which were seen in the bottom of the wound. The spinal accessory and phrenic nerves were both exposed and spared in the dissection.

Postoperative Course.—The patient made an uneventful recovery and was discharged on June 25, 1930, five days after operation. The wound was well healed.

Gross Pathologic Examination.—The specimen, a tumor of the neck, was composed of a large mass of adipose and areolar-looking tissue. In places there was a thin transparent membrane containing or enclosing clear fluid, possibly lymph. There was no structure present resembling a definite distended cyst or tumor. The walls of the cysts had largely collapsed.

Microscopic Examination.—A large block of tissue was preserved for microscopic study.

Low Power: The section showed numerous irregularly shaped, small and large, partially collapsed cystic spaces, surrounded by thin walls of irregular thickness lined by endothelial cells (fig. 38). The stroma of these walls was extremely delicate. There was a small amount of fine, fibrillar groundwork and the striking finding was the large cord of lymphoid cell accumulations, which made a kind of central core running down the length of the walls. There were many blood vessels, varying in size from the fine capillaries to vessels of fair size, in this lymphoid tissue and in the walls proper. In the outer portions of the tissue appeared the usual fine fibrillar stroma, in which there were great numbers of small blood and lymph spaces and the delicate, areolar reticular tissue previously described. In this portion of the tissue there were seen the beginnings of lymph follicles.

Fig. 38 (case 7).—A low power photomicrograph (× 9) of a section of a multiloculated hygroma. Several large cystic spaces, partially collapsed, are seen in the center. The walls are slender and of varying thickness. Masses of lymphoid cells in the form of cords are seen running in the center of the walls and throughout their length. Above and below in the section, one sees the characteristic hygromatous stroma.

High Power: The cell walls were lined by a well preserved and demonstrable endothelium; below the endothelium was a zone composed of loosely meshed fibrillae of fine, wavy, light-pink-staining connective tissue. There was a thick central zone often running a considerable distance in the wall and filled with a dense accumulation of deeply staining lymphoid cells, epithelioid cells and large light-staining cells, which were probably lymphoblastic, such as are seen in the germinating centers of lymph follicles (fig. 39). Numbers of polynuclear cells and pale-pink-staining plasma cells were also seen. The lymphoblastic germinal centers were strikingly absent in this vascular lymphoid tissue. In some areas this

lymphoid cell core was itself covered by endothelial cells. In the outer portions of the section were large areas of extremely fine, delicate stroma. Minute fibrillae divided small, irregularly hexagonal areolar spaces; at the point of intersection of the fibrillae appeared the typical three-cornered cell, with a small amount of protoplasm and a well staining nucleus. In some ways this tissue, which was largely the ground stroma, resembled a very delicate adipose tissue. This condition was so common in the tissue in this case and in other cases described that it seems to be characteristic of the hygromatous stroma. There were also numerous blood vessels, lymphoid cell cords, lymph spaces and cells of various types in this stroma. The lymphoid cell predominated, however. There were some polynuclear cells and also some lymphoblastic cells. The tissue appeared to be young and growing. The diagnosis was hygroma colli cysticum.

Fig. 39 (case 7).—A photomicrograph (× 50) of the area enclosed in the circle in figure 38. Dense aggregations of lymphoid cells are seen, forming a central core within the walls of the cysts. Numerous small blood vessels are seen in this lymphoid tissue. Germinal centers, often found in hygromatous tumors, are here absent.

Follow-Up Notes.—July 7, 1930: Numbness was present over the upper part of the thorax and the lower part of the back.

Sept. 15, 1930: There were occasional sharp shooting pains through the right shoulder.

Oct. 2, 1931: No evidence of recurrence appeared. There was a very slight residual weakness of the right arm; this was much improved over the condition present before operation, however. The reflexes were normal. There was no evidence of the trigeminal rhythm which was present before operation.

May 6, 1933: The pain radiating to the back of the neck and right ear had been relieved. The paresthesia of the right hand and fingers, "falling asleep," had

disappeared. Heart sounds were clear and regular. The pulse rate was 76. Local examination showed a linear scar over the right posterior triangle. The feeling of choking and difficulty in swallowing previously present at times had been relieved. There was no evidence of recurrence. Slight weakness had persisted in the right arm. The weight was 203 pounds (92.1 Kg.). The result appeared satisfactory approximately three years after the operation.

CASE 8.—R. K., a boy, 3½ years of age, was admitted to the Long Island College Hospital on March 6, 1931, because of a swelling in the right axilla of eight to nine months' duration. He was discharged March 20.

History.—The child was born by a normal delivery at full term. There was no history of serious illness or acute infectious disease. There had been no loss of weight. Ten months before his admission, when he was 2½ years old, his mother noticed a fulness in the right axilla. This swelling increased slowly in size, was not painful and did not trouble the child. It had been aspirated by the family physician five months previously. Some fluid was withdrawn, and the fulness temporarily subsided. Shortly before admission there had been a return of the swelling, which at the time he was seen was as large as half an orange.

Examination.—The patient was a well developed white boy, in good general condition. A general examination revealed no abnormal findings other than those referable to the right axilla. There was a soft, cystic, lobulated swelling or fulness, the size of half an orange, which obliterated the cavity of the right axilla. There was no redness of the overlying skin, and the tumor was not tender. It was adherent to the skin and to the deep tissues of the axilla and chest wall. There was no interference with the movements of the arm.

The temperature was 100 F., the pulse rate 110 and the respiratory rate 20. The erythrocyte count was 4,850,000, the hemoglobin content 86 per cent and the leukocyte count 8,400. There were 79 per cent polymorphonuclears and 21 per cent small and large mononuclears. The examination of the urine gave negative results. There was a preoperative diagnosis of hygroma of the right axilla.

Operation.—On March 11, with the patient under ether anesthesia, an incision was made parallel to the right anterior axillary line, thus exposing the hygromatous tumor. Dissection was carried anteriorly, liberating the tumor from the pectoral muscle and the deep subcutaneous tissues. Posteriorly the tumor was dissected free and separated from the serratus anterior, latissimus dorsi and subscapular muscles. The long thoracic nerve was seen traversing the medial portion of the tumor, and was carefully preserved. The intercostohumeral nerves were also spared. In an upward direction, the cystic tumor was attached by an apparent pedicle to the axillary vein and the proximal portion of the subclavian artery. After division of this stalk, the tumor was completely extirpated. It was multilocular and cystic and contained a clear watery fluid.

Postoperative Course.—The child made an uneventful recovery and was discharged March 20, 1931, nine days after operation.

Gross Pathologic Examination.—The specimen was a tumor from the axilla. It had been incised and the watery contents lost. The walls were of varying thickness. The inner surface was glistening, smooth and multilocular. Subcutaneous tissue and muscle were seen overlying the outer surface of the cystic tumor.

Microscopic Examination.—The greater part of the tumor was made up of small spaces lined by one or two layers of flattened cells. Coursing through it in various directions were bands of delicate fibrillar stroma, containing relatively large thin-walled blood vessels. Other areas of the tumor showed spaces enclosed in relatively thick walls and presenting the general structure of lymph sinuses.

Section 1. Low Power: A large, representative block of tissue showed an extremely delicate, loose, lacelike architecture, produced by folded and collapsed thin walls lining irregularly shaped large and small cyst spaces. The thin and delicate walls were lined by endothelium and composed of a finely reticulated fibrillar meshwork of connective tissue, such as was seen in previous cases. In one cyst a cross section of a process which is entirely composed of this reticular tissue was seen. It resembled an extremely fine adipose tissue. Some of the walls were older and fairly densely fibrotic.

High Power: The walls lining the cystic compartments were of varying thickness. Some of the thicker ones were composed of a fairly dense, wavy, hyaline, pink-staining connective tissue, containing few nuclei and numbers of lymphoid and epithelioid cells. The thinner walls were far more delicate in structure. They were more open and porous and composed of a loose, areolar, reticular framework which contained many small blood vessels and small aggregations of lymphoid and lymphoblastic cells, as well as epithelioid cells and occasional granular cells. The walls were everywhere lined by clearly stained endothelial cells. In the walls were seen connective tissue fibrillae, a few tissue cells and lymphoid and lymphoblastic cells. Here and there a small amount of adipose tissue was seen together with an occasional early beginning of a lymph follicle. The section was principally characterized by the extremely fine, thin cyst walls.

Section 2: This section was composed of a spongy tissue enclosing numerous spaces (fig. 40). There were several large blood vessels, both arteries and veins, and several fairly large irregularly shaped lymph spaces containing a coagulated secretion which stained lightly pink. The walls were fairly thick and composed of hyaline connective tissue. There was the usual well defined lining of endothelial cells. A few nerve fibers were seen. This section illustrated the rather marked vascularity of the hygromatous stroma which, in the form of a delicate, extremely fine, areolar network, surrounded this area. Another field showed a second large spongy area consisting almost entirely of small, irregular collapsed cyst spaces. The walls of the smaller spaces in this instance were dense and hyaline and contained a fair number of connective tissue nuclei, indicating, probably, a growing area. There were few blood vessels present. These small cyst spaces with heavy connective tissue walls contrasted strikingly with the very delicate meshy walls described in the first section discussed. Lymphoblastic cells were seen in the stroma around this area.

Section 3: This section resembled in many respects the two already described and showed even better the extreme fineness of the walls of many of the larger cysts (fig. 41). These walls, lined by endothelium, were composed of a delicate subendothelial connective tissue layer. The remainder of the wall was composed of the characteristic extremely fine areolar reticular connective tissue. Frequent occurrence of small blood vessels is also noted. Certain areas of heavy, dense, hyaline connective tissue trabeculae are seen. Papillary proliferations projected into cyst spaces, which in general were enclosed in a loose, meshy, hygromatous connective tissue of the fine areolar type. Lymphoid tissue and lymphoid follicles were conspicuously absent in this section. The diagnosis was hygroma.

Follow-Up Note.—May 6, 1933: No answer to the questionnaire was received. The patient could not be traced.

CASE 9.—C. F., a mulatto girl 5 years of age, was admitted to the Long Island College Hospital on Feb. 14, 1932, because of an infection of the upper part of the respiratory tract and swelling of glands of the neck. She was discharged April 15.

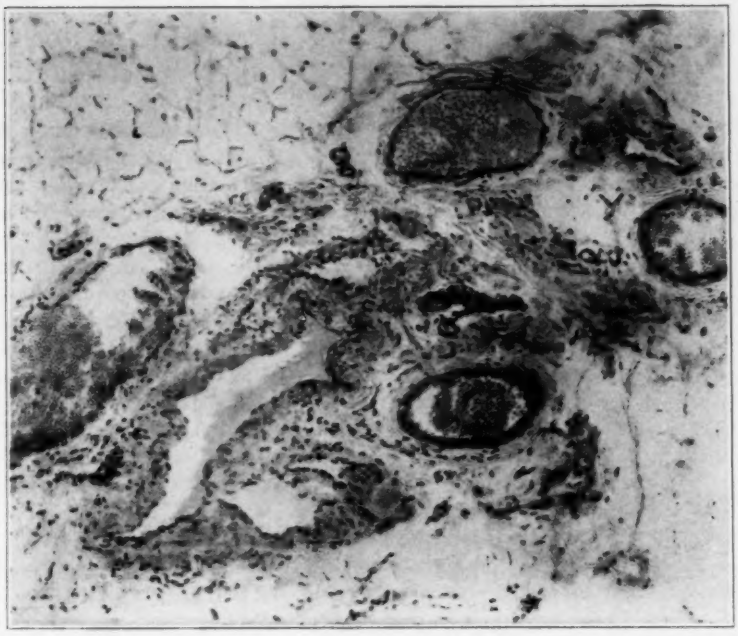

Fig. 40 (case 8).—A photomicrograph × 85) of a section illustrating the marked vascularity which is often noted in the stroma of hygromatous tumors. One large cyst with a thick fibrous wall and several small cysts are seen. The stroma presents the characteristic meshy lacelike appearance.

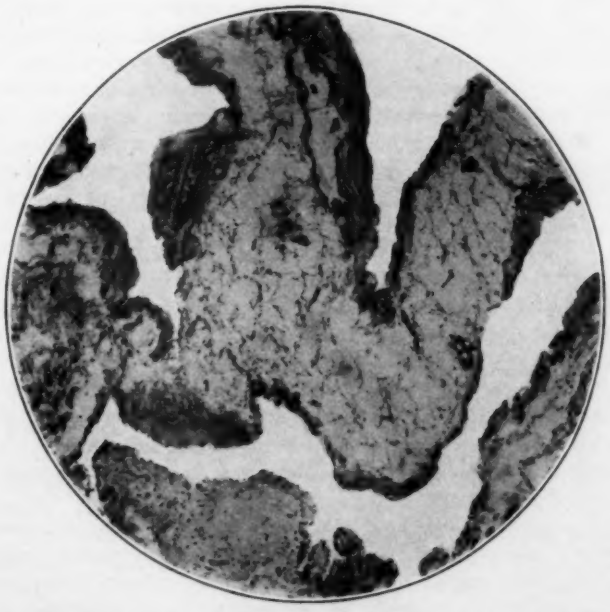

Fig. 41 (case 8).—A photomicrograph (× 50) of a section illustrating the delicate structure of the walls of the larger cysts in some instances. They are, for the most part, composed of an extremely fine, areolar, reticular stroma of lacelike appearance. The walls of this structure, when viewed in the gross specimens of hygroma, are semitransparent. Lymphoid cell masses are conspicuously absent. In certain areas there is a thickened subendothelial layer of hyaline connective tissue.

History.—The child was a "blue baby" and at birth weighed 10 pounds and 11 ounces (4847.76 Gm.). The delivery was at full term and normal. On her back was a supposed hematoma, which was drained. During the first few months, the draining wound kept the child below par. However, she gradually gained in strength and after the first year had very good health. A large swelling on the right side of the neck was seen at birth. It gradually increased until it reached the size of a grapefruit when the child was 3 weeks of age. The mass produced definite respiratory obstruction, which necessitated incision and drainage. The wound continued to drain for several weeks. Thereupon the swelling became much larger and more localized but did not produce respiratory embarrassment. During the succeeding years, the tumor diminished in size, and when the child was 4 years old it was as large as a lemon. After tonsillectomy at that time, the mass was said to have disappeared altogether. On February 10 the patient suffered an infection of the upper part of the respiratory tract, and soon thereafter the mother noticed a swelling at the site of the old trouble. Since that time there had been a gradual increase in size and extent of the mass. At no time had there been any external rupture with drainage. The temperature was intermittent, low in the mornings and as high as 103 to 104 F. every afternoon. The swelling noted at the time of admission resembled very much the enlargements described in previous cases.

Examination.—The patient was a fairly well nourished girl appearing pale and chronically ill. The skin was hot and moist. The cervical nodes on the left side were not palpable. The axillary and inguinal nodes were palpable. The head appeared massive in proportion to the remainder of the body. There was a tumor about half the size of a grapefruit on the right side of the neck, extending from the lobe of the right ear downward to the supraclavicular fossa. Anteriorly it extended 2 cm. beyond the midline, and posteriorly, to a corresponding distance. The mass was firm and elastic except for several soft cystic areas which were palpated in the lower portion of the tumor. The overlying skin was tense, pinkish at the borders of the mass and darker and adherent over the center. There was no tenderness. Several discrete nodules were felt in the mass. There were three short scars in the skin overlying the swelling. The trachea was displaced 3 cm. to the left. The mass itself did not seem to extend over the mandible but continued behind the ear and posteriorly to the lateral border of the sternocleidomastoid muscle and upward to about the middle of the helix. It filled the right side of the neck down to the middle of the clavicle. There was some limitation of movements of the head and neck caused by the size of the mass. The right side of the neck was definitely warmer than the left. The teeth were in poor condition, and the gums were spongy and infected. The tongue was coated, and the mucous membranes of the mouth and throat were beefy red and much inflamed. The mass on the right side of the neck had caused a bulging of the wall of the pharynx.

The following diagnosis was made in the pediatric department: (1) Vincent's angina or infection of the upper respiratory tract and (2) branchial cleft cyst with secondary infection.

The temperature for the first four days after admission varied between 100 and 103.8 F.; the pulse rate was 100 to 110, and the respiratory rate, 20 to 22. The erythrocyte count was 3,930,000, the hemoglobin content 56 per cent and the leukocyte count 26,950. There were 88 per cent polymorphonuclears, 10 per cent large and small lymphocytes, no mononuclears, no eosinophils and 2 per cent transitional cells. Wassermann and Kahn blood tests were negative. A culture of material from the throat taken on February 15 was negative for Vincent's organisms. However, a pure culture of hemolytic streptococci was obtained. A roentgen

examination on February 16 was reported as showing the following picture: "The trachea is displaced slightly to the left. The heart is definitely enlarged both to the left and right. There is a large upper mediastinal mass on the right side protruding into the lung field, and there is also a soft tissue mass in the right cervical region which is apparently continuous with the mass extending into the mediastinum."

Note: The patient presented a problem in diagnosis. There seemed to have been a recent rapid increase in the size of the mass on the right side of the neck. There was a persistent rather high temperature. The mass had a peculiar, edematous character and pitted on pressure. There was some reddening of the overlying skin, and on account of the previous history of infection of the upper respiratory tract and throat it was thought that there might have been a secondary lymphatic infection in the tumor producing acute adenitis and abscess. At operation, however, as will appear, no gross evidence of infection was found.

Operation.—A partial extirpation of a hygroma of the right side of the neck was performed on February 19 with the patient under ether anesthesia. Thinking that the condition might be of inflammatory nature, I made a small conservative incision over the center of the mass. It soon appeared that the tumor might be neoplastic. The incision was then increased in extent and by means of the finger, a cystic, lobulated tumor was partially circumscribed, after which a considerable amount of lymph escaped. There were dense, firm adhesions everywhere, indicating an old chronic process. Finally, a mass as large as a lemon situated in the upper anterior triangle was separated from the main tumor and removed. The dissection was continued downward to the level of the clavicle, where a large number of thin-walled lymphatic cysts were seen extending into the mediastinum. Because of the adhesions and the great number of large, fragile veins in this area, no attempt was made to extirpate the tumor. On further exploration, it was found that the tumor extended into the submaxillary and submental areas, into the tonsil bed, forward to the floor of the mouth and downward into the anterior triangle. Because of the wide extent of the tumor, extirpation of these extensions was deemed inadvisable.

Postoperative Course.—February 19 to 24: A summary of this period reveals the following information. The child was definitely ill. The temperature rose to 103 F. An icteric tint developed in the scleras and in the skin and continued to deepen in color. The throat was much reddened and injected. Examination of the lungs gave negative results except for mediastinal dulness extending 2 cm. to the right of the sternum. Repeated examinations showed that the liver was gradually enlarging. The splenic edge was palpable. A roentgenogram of the chest revealed an increase in the size of the mass in the upper mediastinum and right side of the chest. The diagnosis of acute hepatitis with jaundice was made by the pediatricians in attendance. A transfusion of 180 cc. of citrated blood was given on February 22.

February 24: A roentgen examination showed that the mediastinal mass and the heart were larger than on the previous examination (fig. 47 *A*).

February 25: Temperature of the septic type had continued. The mass on the right side of the neck just below the angle of the jaw had increased in size. Examination of the lungs revealed an early pneumonic process in the upper part of the right lung, and signs of beginning pneumonia were noted in the posterior infrascapular region on the right.

February 27: The urine showed a trace of albumin, numerous white blood corpuscles and the presence of bile.

February 28: The blood culture was sterile.

February 29: A roentgen examination showed that the tumor had increased slightly in size as compared with the findings on the previous examination. The splenic tip had descended 2 cm. and was firm.

March 1: The tumor had increased markedly in size, especially behind the ear. On account of the marked anemia, a transfusion of 200 cc. of citrated blood was given. The roentgen diagnosis was a tumor, cervical and mediastinal, presumably malignant, on the right side, and cardiac enlargement. Roentgen therapy to the tumor was advised by Dr. A. L. L. Bell.

March 4: The temperature continued to be of the intermittent septic type. The tumor continued to increase in size, especially just below the ear and extending posteriorly below the occiput. The right ear drum was red and bulging. Jaundice was still marked.

March 5: There was a mass of infiltrated glands at the angle of the right jaw. This was exerting lateral pharyngeal pressure. The clinical diagnosis of acute suppurative lymphadenitis or lymphosarcoma and otitis media suppurativa was made. Paracentesis and drainage of the middle ear were advised.

March 6: For three days considerable edema and an area of fluctuation had been noted posterior to the operative incision. Six or eight cubic centimeters of a clear, yellow fluid which clotted quickly was withdrawn by aspiration. Since operation the wound had been discharging large amounts of serous fluid and had shown little tendency to heal. Between March 7 and 13, four exposures to high voltage roentgen rays were given to the tumor, which was tentatively regarded as a lymphosarcoma.

March 9: There had been some improvement since the roentgen therapy was instituted. The jaundice had diminished. The tissues of the neck were less boggy, and there was a noticeable decrease in the size of the swelling.

March 13: A transfusion of 180 cc. of citrated blood was given. Early pneumonic involvement of the middle lobe of the right lung was revealed by roentgen examination.

March 14: A roentgen examination revealed that the cervical mass was definitely smaller than it was on the previous examination.

March 15: The sixth roentgen treatment was given. The plate showed an increase in the pneumonic process with a definite fluid layer in the general pleural cavity on the right. The jaundice was less intense, and the liver was somewhat smaller. The general condition of the patient was fairly good.

March 16: A roentgen examination showed that the upper mediastinal shadow was still of considerable size. The conclusion from the roentgen findings was as follows: "While the lymph node in the cervical region has responded satisfactorily to radiation, and the upper mediastinal mass has responded to some extent, there seems now to be present a pneumonic process with a pleuritis on the right side. There is an increase in the mediastinal shadow due probably to fluid surrounding the tumor. For the time being at least, roentgen therapy must be discontinued." A diagnosis of sarcoma, cervical and mediastinal, and pneumonia was made.

March 17: The anemia had increased; the erythrocyte count was 2,970,000, the hemoglobin content 58 per cent and the leukocyte count 14,000. There were 88 per cent polymorphonuclears, 11 per cent large and small lymphocytes and 1 per cent mononuclears.

March 19: Since roentgen therapy was begun the tumor on the right side of the neck had markedly diminished in size. The collection of fluid on the right lateral and posterior aspects of the neck had almost disappeared. The operative wound was closing.

March 20: A culture of the sputum showed hemolytic streptococci predominating.

March 26: The erythrocyte count was 3,180,000, the hemoglobin content 65 per cent and the leukocyte count 11,000. There were 70 per cent polymorphonuclears, 28 per cent large and small lymphocytes and 2 per cent mononuclears.

March 20 to April 11: During this interval seven roentgen treatments were given. The anemia continued.

April 6: The culture of the fluid aspirated from the fluctuant area over the tumor yielded hemolytic streptococci.

Gross Pathologic Examination.—The portion of the tumor removed at operation was as large as a lemon and presented an irregular, ragged surface. On section the greater part of the specimen showed dense irregular masses and bands of scar tissue coursing in all directions. Between these bands were cystic or tubular channels lined by a smooth, glistening membrane and a spongy tissue somewhat resembling in structure the common rubber bath sponge. The cystic spaces were enclosed in thin, transparent walls. The specimen contained one firm nodule the size of an English walnut, which was composed largely of fibrous tissue and fat. In one area the specimen had a smooth, semitranslucent appearance caused by a group of edematous lymph nodes. Between the cysts in the outer border of the tumor could be seen large blood vessels of varying size. Purulent exudate or other evidence of gross infection was not found.

Microscopic Examination.—Because of the varying character of the different portions of the tumor, four representative blocks of tissue were preserved for microscopic examination.

Block I. Low Power: One margin of the section was formed by a thick connective tissue wall composed of wavy fibers, between which there had been infiltration of large numbers of cells (fig. 42). Immediately below this wall was a large zone of cystic spaces, many of which were filled with coagulated secretion in which were dense accumulations of cells. The walls separating these cellular areas were also infiltrated with cells. Distant from this area were many cystic spaces lined by thin, delicate walls; there the coagulated contents appeared clear and were almost devoid of cells. The intervening walls were of loose, fine, meshy structure and contained many small blood vessels and numbers of lymphoid cells. The lining membrane of the cyst spaces was smooth and glistening. Here and there were seen areas of loose, areolar structure, such as were seen in previous instances. The walls separating these small spaces were infiltrated with cells. The spaces themselves were free from contents.

High Power: In the wavy connective tissue of the outer wall were many large and small mononuclear and polymorphonuclear cells. Epithelioid and spindle-shaped cells were also present in large numbers. Numerous large lymphoblastic cells were seen. Areas of areolar reticulum were seen in the wall and in the surrounding stroma. In the spaces thus formed appeared a great variety of cells—large mononuclear, relatively pale cells, large spindle-shaped cells with irregular contracted nuclei, epithelioid cells, large protoplasmic cells with one or more huge nuclei, lymphoid cells, polymorphonuclear and polynuclear cells. Small blood vessels were common. In general there was a multiplicity of cells, which varied, as did their nuclei in size and shape. The latter were generally rich in chromatin. In one large area there were in addition to those cells present in the walls proper, an enormous number of polymorphonuclear cells in the coagulated secretions of the cysts (figs. 43 and 44). One could also see lymphoid and lymphoblastic cells and some red corpuscles. (There was evidently a secondary infection from the

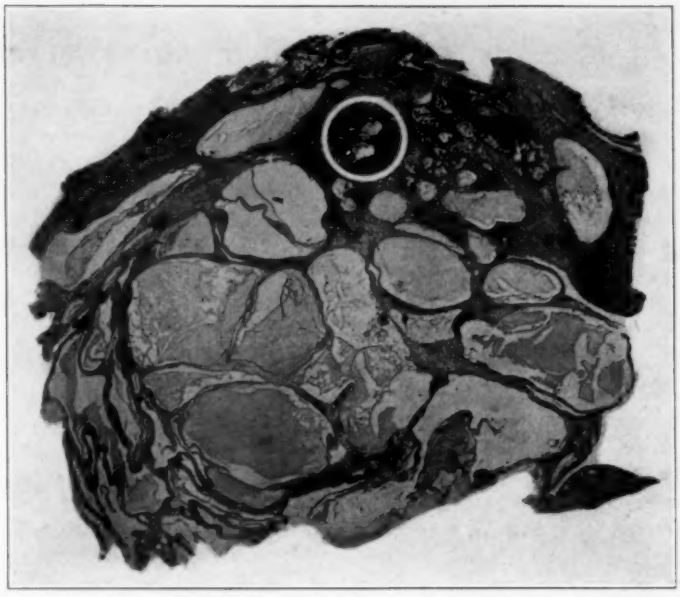

Fig. 42 (case 9).—A photomicrograph (× 7) of a section of hygroma, showing inflammatory reaction due to secondary infection with the hemolytic streptococcus derived from an "acute sore throat." In the upper right field the walls and cavities of the cysts are densely infiltrated with cells of inflammatory origin. The noninfected cysts in the lower field are clear and well defined, and their walls are extremely fine and delicate. The area enclosed in the circle is shown in higher magnification in figure 43.

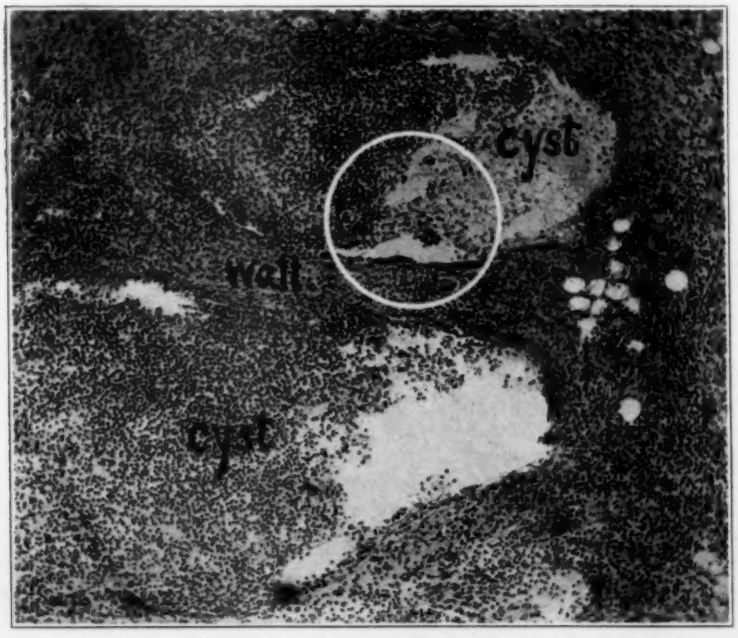

Fig. 43 (case 9).—A photomicrograph (× 75) of the area enclosed in the circle in figure 42. The two cystic cavities and the intervening wall are densely infiltrated with cells of inflammatory origin.

throat.) Farther away from this cellular zone, the walls of the cyst spaces presented more of the usual picture (fig. 42). There the delicate connective tissue fibrillar structure was again seen. The predominating cells were the large and small mononuclears, which were regarded as the lymphoid and lymphoblastic cells. There were many epithelioid cells also. The cysts were lined by endothelium. Here and there were seen small aggregations of lymphoid cells, but true follicles were not seen. Small blood vessels were common. The coagulated secretion of these cysts was practically clear and contained only an occasional lymphoid and polymorphonuclear cell.

Block II. Lower Power: The section consisted of two main parts, a heavy zone of rather dense connective tissue of wavy character, between the fibrillae of which occurred numerous lymphoid cells, leukocytes and red corpuscles, and a large area

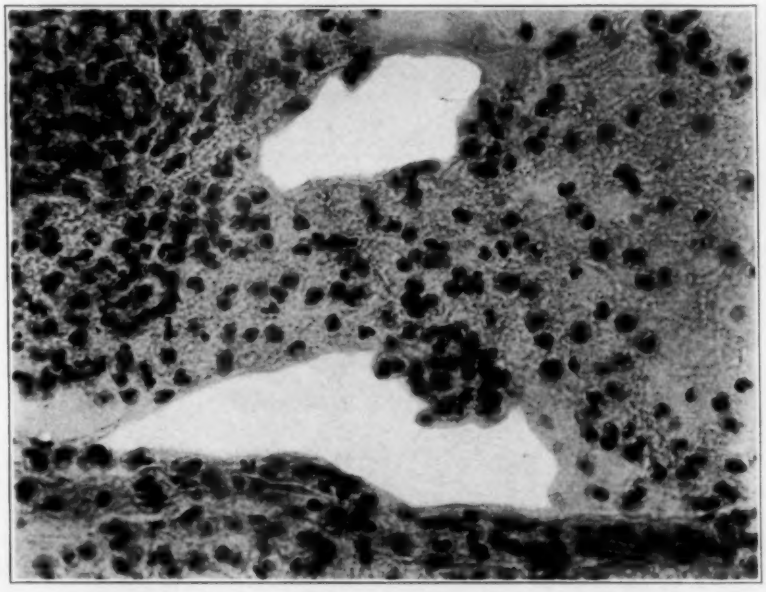

Fig. 44 (case 9).—A photomicrograph (× 400) of the area enclosed in the circle in figure 43. Note the numerous polymorphonuclear and large mononuclear cells in the cyst wall below and in the cavity of the cyst.

of cyst spaces, in the walls of which occurred dense accumulations of lymphoid cells. The whole had a spongy appearance (fig. 45).

High Power: The outer connective tissue wall was broad and thick, composed of meshy hyaline and pink-staining tortuous fibers, between which were numerous cells of all types—the lymphoblastic cells, polymorphonuclears, spindle-shaped connective tissue cells and others of various bizarre irregular shapes. In the zone of small cyst cavities the walls were fairly thick. There was a fine fibrillar groundwork. The connective tissue cells were spindle shaped. In the walls and in the stroma were large numbers of the huge lymphoblastic cells with very large nuclei, also polymorphonuclear cells, lymphoid cells and at intervals numerous dense aggregations of lymphoid cells but apparently no true follicles (fig. 46). Numbers of polymorphonuclear cells were everywhere seen.

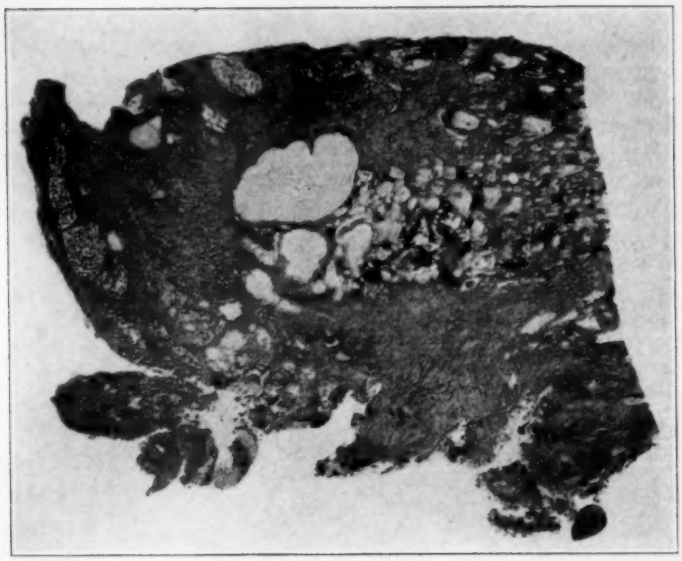

Fig. 45 (case 9).—A photomicrograph (× 7) of a section illustrating the spongy stroma often seen in hygroma. Note the innumerable small cysts and the broad zones of dense fibrous tissue below and to the left. The very dark areas between the cysts represent areas of lymphoid cell aggregations in the walls of the cysts.

Fig. 46 (case 9).—A photomicrograph (× 75) of a section from the zone of small cysts shown in figure 45. The spongy character of the tumor, the lymphocytic infiltration in the walls of the cysts, and the denser accumulations of lymphoid cells are well shown. Germinating centers are not seen in this section.

Block III. Low Power: The section in general showed the fibrillar structure of the loose connective tissue ground substance, in the meshes of which occurred the various types of cells just described. The principal structures in the remainder were the large, dense cellular aggregations lying in the cyst cavity, composed principally of polymorphonuclear cells.

High Power: The long, spindle-shaped, wavy connective tissue fibrillae were well shown, containing the typical spindle-shaped nuclei. In the spaces between the fibrillae occurred various types of cells such as those just described. There was one large cyst space which was completely filled, principally with dense accumulations of polymorphonuclear cells. In addition, coagulated secretion, some large mononuclear and lymphatic cells and a sprinkling of lymphoid cells were found. Red corpuscles were also seen.

Block IV. Low Power: This large block was composed entirely of spongy tissue with relatively small cyst spaces of fairly uniform size. A few large accumulations of lymphoid cells were seen. Similarly some of the cyst walls had dense aggregations of lymphoid cells but no true follicles. The walls were fairly thick.

High Power: In the cyst walls the predominating types of cells were the large mononuclear cells with huge nuclei showing a clear nucleolus and very little protoplasm. Nuclei were relatively pale and highly granular. These were possibly lymphoblastic cells. Then there were fairly numerous, large eosinophilic granular cells with very large rounded nuclei. Epithelioid cells were common, as were the irregularly spindle-shaped nuclei in those cells with little protoplasm. In fact, almost every type of cell was seen. There were numbers of small capillaries everywhere. Because of this great variability in the cellular and nuclear shapes and sizes, the possibility of malignancy was considered. Karyokinetic figures, however, were not common. The usual endothelial lining of the cyst spaces was seen.

The pathologic diagnosis was hygroma cysticum, secondarily infected, with possibility of malignancy. The presence of lymphosarcoma was questioned.

Comment.—The child came into the hospital with an infection of the upper respiratory tract. This subsequently developed into streptococcic pharyngitis, otitis media and pneumonia. Positive cultures of Streptococcus haemolyticus were repeatedly obtained. Secondary acute cervical adenitis with abscess was suspected in the further course, and it was only after surgical exploration that the diagnosis of hygromatous tumor with infection was made. Gross infection was not found, but the results of incidental infection were well shown in the microscopic study of the hygromatous tumor removed at the time of operation. This was the only case in the series in which there was complicating incidental acute infection. The possibility of lymphosarcoma was suggested by Dr. A. L. L. Bell in the roentgenology department. Eleven treatments with high voltage roentgen radiation were given the hygroma during the patient's stay in the hospital.

Follow-Up Notes.—After leaving the hospital the patient received roentgen treatments over the mediastinum anteriorly and posteriorly. Two treatments per week were given over a period of six weeks. A roentgenogram taken at the end of the period of treatment showed a marked diminution in the size of the mediastinal growth. About two months later another film showed still further improvement and a very satisfactory appearance of the mediastinum (fig. 47 *B*). Other than this, the patient received no special treatment. She was 7 years old at the time of the examination.

May 11, 1933: About fourteen months after operation the child was growing, and gaining weight. On discharge from the hospital she weighed 33 pounds

(15.0 Kg.). At this examination her weight was 57 pounds (25.9 Kg.). A moderate pallor of the mucous membranes and face persisted.

Local examination showed an irregular, depressed scar running along the anterior border of the sternocleidomastoid muscle. There was no apparent swelling. A slight fulness was noted in the submaxillary space on the right as compared with the left side. There were several enlarged lymph glands to be felt in the submaxillary space. These glands were discrete and fairly firm. There was no mass and no cystic swelling anywhere. There was no enlargement of the glands in the anterior or posterior triangle on the right. On the left a few small glands were felt in the anterior triangle. The note over the manubrium was resonant to percussion.

There was some gingivitis, and the patient had lost several teeth. This was attributed to the numerous roentgen treatments. There was no bulging of the larynx, and examination of the throat gave negative results. There was no dyspnea, and

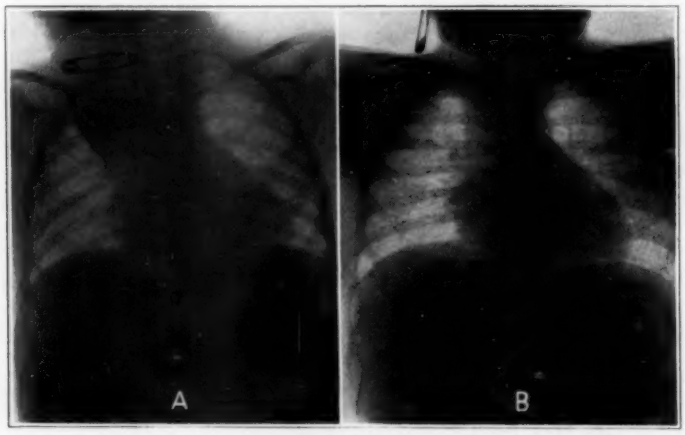

Fig. 47 (case 9).—*A*, roentgenogram of the neck and mediastinum taken on Feb. 24, 1932, before irradiation. The enlargement of the neck on the right side and the mediastinal shadow caused by the hygromatous tumor are clearly displayed. *B*, roentgenogram taken seven months later, on September 26. Prolonged and relatively intense high voltage roentgen therapy had been given. The photograph shows the diminution in the enlargement of the right side of the neck and in the extent of the mediastinal shadow as compared with the findings in *A*, before irradiation.

the voice was clear. The heart sounds were clear, and the pulse rate was 92 and regular.

There was no evidence of recurrence of the old condition. One point of possible significance was the fact that there was a group of moderately enlarged glands in the right submaxillary space. There was no edema or fulness of the tissues at the back of the neck.

The appetite was good. The child was active and appeared in good condition.

Case 10.—D. S., a boy 16 months of age, weighing 22 pounds (9,979.02 Gm.), was admitted to the Long Island College Hospital on Nov. 5, 1925, and discharged on November 15. He had been born with a lump on the right side of his neck. This mass increased in size when he was a year old.

History.—The delivery was at full term and normal. He nursed well and gained weight normally. The general health had always been good. At birth a tumor the size of a hazelnut was noticed just below the angle of the jaw on the right. This tumor remained stationary in size for almost one year. After that time there was gradual enlargement, until the growth became as large as a hen's egg. The tumor had always been soft and had never been painful or tender.

Examination.—The child was well developed and well nourished, of good color, normally active and able to walk and talk. The anterior fontanel was practically closed. In the posterior triangle on the right side of the neck there was an oval swelling extending posteriorly almost to the midline, upward to the base of the skull and anteriorly to the external auditory meatus, the angle of the jaw and the sternocleidomastoid muscle. The swelling was approximately the size of a large egg and measured in vertical diameter 8 cm. and in transverse diameter 7 cm. It was definitely soft, not discolored, fluctuant and slightly tense and gave the impression of containing fluid. The overlying skin was unusually thin and through it one could see a bluish reflex. There was no tenderness. In the midposterior margin of the tumor one could feel a hard nodule the size of a hazelnut, which was attached and could not be shifted about. This gave the impression of a hard, enlarged and somewhat tender lymph gland. There were no other glandular enlargements on either side of the neck. One could notice an asymmetry of the mouth, which was drawn downward and to the right by the tension of the tumor. This was particularly noted when the child cried. The pulse was rapid, regular and of good volume and tension. Otherwise the general physical examination gave negative results.

The temperature was 98.8 F., the pulse rate 112 and the respiratory rate 24. The erythrocyte count was 4,960,000, the hemoglobin content 90 per cent and the leukocyte count 16,200. There were 68 per cent polymorphonuclears, 28 per cent small mononuclears, 3 per cent large mononuclears, and 1 per cent eosinophils. The examination of the urine gave negative results. The preoperative diagnosis was hygroma, lymphangiomatous tumor.

Operation.—The hygroma was excised on November 16, with the patient under ether anesthesia. Lenticular incisions were made over the mass to include an area of thin atrophic skin which was not considered viable. Dissection was begun posteriorly and carried downward, finally exposing a rather firmly adherent splenius capitis muscle. A thin-walled sac appeared and was punctured, whereupon a lymphlike fluid escaped. The operation was then continued anteriorly, exposing the scalenus medius and the posterior border of the sternocleidomastoid muscle. Below the inferior surface of the exposed mass the branch of the spinal accessory nerve to the trapezius muscle was exposed. Finally the cystic tumor was dissected downward to form a pedicle, which was attached at the junction point of the subclavian and jugular veins, but no evident communication was found. This pedicle was divided. A cigaret drain was placed.

Postoperative Course.—November 8 to November 15: The patient's convalescence was uneventful; the wound healed normally and he was discharged in good condition.

Gross Pathologic Examination.—The specimen, a cystic tumor of the neck, was smooth and elastic and approximately as large as an egg. Two large, thin-walled, multilocular cysts, measuring 3 cm. in diameter and containing clear fluid, were seen. When the cystic mass was opened, the contained fluid, resembling blood serum, escaped. Numerous irregular fibrous bands were seen to extend in various directions along the inner aspect of the confining walls. In the wall of one of the

cysts at the base of the tumor, a small irregular body, 1 cm. in diameter, was seen. It had a vascular spongy appearance, and from its cut surface blood could be expressed. It was identified as a hemolymph gland. Strands of fibrous tissue extended in a radial direction from the center of the tumor to its capsule. Lying between these trabeculae were lobules of spongy-appearing tissue. Blocks were taken from the tumor proper and from the walls of the cysts for microscopic study.

Microscopic Examination.—The outer cyst wall was composed of fibrous tissue, covered by a thin layer of muscle and lined on its inside by a single layer of endothelial cells. The tumor proper was composed of a mass of loculated connective tissue, containing large numbers of cystic spaces and numbers of blood vessels of varying size. A spongy type of connective tissue surrounded the blood and lymph spaces. The diagnosis was hygroma.

Second Admission.—Soon after the operation done on November 16, the neck increased in size because of a cystic swelling in the right submaxillary region. This swelling gradually became larger until it resembled the tumor removed at the previous operation. On April 10, 1926, there was a large, bulging, soft, fluctuant swelling, resembling the original tumor, occupying the area below the ear and the angle of the jaw and extending into the submaxillary triangle. It was approximately 2 inches (5 cm.) in horizontal diameter and ¾ inch (1.9 cm.) in transverse diameter. The mass felt cystic, and there were no nodules palpated in it. A general physical examination gave the same results as before. There had been no recurrence of the tumor in the area of the former operation. The clinical examination gave negative results.

Operation.—A secondary excision of the hygroma was performed on May 3 with the patient under ether anesthesia. The operative procedure was confined to the right anterior triangle, whereas the former operation was carried out in the posterior triangle. The dissection was long and tedious. The tumor was unusually extensive, having penetrated between and along practically all the important structures in the anterior triangle. The necessary dissection finally exposed the anterior jugular vein, vagus nerve, carotid artery, deep cervical lymph nodes and hypoglossal nerve and anteriorly the thyroid gland, to which the tumor was attached. The cystic mass extended above into the submaxillary space and posteriorly to the tip of the parotid gland, the mastoid process, the sternocleidomastoid muscle and the old scar. It was attached to, and involved, a large group of lymph glands in the deep midportion of the neck. These glands were removed with the tumor. The mass extended downward almost to the level of the clavicle in the form of a pedicle, which contained a large number of edematous-looking lymph glands. A thorough and extensive resection was done before it was felt that all the tumor had been removed. Another small cystic mass, which was enucleated from the submaxillary area and which seemed separate from the main tumor, was found to involve the submaxillary lymph glands. This portion resembled the major tumor. In the dissection of this area the hypoglossal nerve was unavoidably divided and subsequently sutured with fine silk. The wound was closed with drainage. The operation was well borne. An operative diagnosis of hygroma colli cysticum was made.

Postoperative Course.—May 3 to May 6: There was a good recovery from the operation. The protruded tongue deviated to the right.

May 9 to June 12: Acute purulent rhinitis developed, followed by infection of the operative wound, which had to be opened and drained. Culture of material from the wound yielded hemolytic streptococci. Following careful treatment of the wound and supportive measures for the patient, recovery was complete, and the patient was discharged in good general condition on June 12, 1926.

Gross Pathologic Examination.—The tumor removed at operation measured 3 by 3 cm. after the escape of its fluid and was surrounded by muscle, fat and connective tissue. It was of the same appearance and structure as were noted in the original tumor removed at the first operation. The cystic fluid was straw colored and watery and had the appearance of pale urine. The bulk of the tumor was enclosed in a thin, glistening, semitransparent membrane, resembling peritoneum, whereas in other portions the capsular wall was thick, heavy and fibrous. The tumor was multiloculated and contained numbers of thickened trabeculae. (The question of malignancy could not be determined on gross examination and the possibilities of recurrence must be kept in mind.)

Microscopic Examination.—A section through the wall of the cyst was examined. A thin portion of cortex showed a fairly normal lymph gland structure but merged rapidly into an irregular arrangement. The germinal centers were lost or contained projections of lymphoid cells of more mature type. The stroma was markedly increased and irregularly arranged. The next zone was one of dilated lymph sinuses containing very few cells and showing a decrease in stroma. The diagnosis was lymphangiomatous tumor, hygroma.

Follow-Up Notes.—June 27, 1927: One year after the patient's discharge from the hospital, he was examined by Dr. E. J. Browder. He looked well and was growing normally. There was no evidence of recurrence. No palpable nodules were found on the right side of the neck. The tongue protruded to the right. The anterior third of the tongue on the right was atrophic. The mucous membrane on this side was wrinkled from the atrophy of the intrinsic muscles. The posterior two thirds on the right appeared smaller than on the left. It seemed that the deviation was not quite as marked as when the boy was discharged from the hospital about one year before.

May 6, 1933: No answer to the questionnaire was received. The patient could not be traced.

Case 11.—Mrs. A. F., aged 27, was admitted to the Long Island College Hospital on March 22, 1927, because of a swelling of the neck, which it was thought might be a goiter. She was discharged on March 29.

History.—The patient had always been well. The menses began when she was 13 years of age and had always been regular. She had been married seven years and had two children. One year previously, after a cold, a lump appeared over the anterior midportion of the neck. It was the size of a golf-ball. She visited another hospital, where, because it was assumed that the swelling was a goiter, 4 drops of iodine were given three times a day for four months. There had been no symptoms of hyperthyroidism. The tumor caused no symptoms.

Physical Examination.—The patient was a well developed, well nourished, healthy-looking woman. A general physical examination gave negative results. The neck was not enlarged and showed no abnormalities other than a small mass over the anterior midportion midway between the larynx and the jugular notch. It was not sharply defined and covered an area as large as a 50 cent piece. It appeared to be subcutaneous but was attached to the deeper structures. It did not rise with swallowing. The overlying skin was not intimately attached to the tumor. It had a "doughy," collapsible, cystic consistency and was generally circular in shape. There was no redness or tenderness.

Clinical Examination.—The temperature was 98 F., the pulse rate 80 and the respiratory rate 20. The erythrocyte count was 4,350,000, the hemoglobin content 87 per cent and the leukocyte count 11,000. There were 60 per cent polymorphonuclears, 31 per cent small mononuclears and 1 per cent large mononuclears. The examination of the urine gave negative results. The systolic blood pressure was 140 and the diastolic 60.

Operation.—The hygroma of the neck was excised on March 23, 1927, with the patient under nitrous oxide and ether anesthesia. A transverse incision was made over the most prominent portion of the swelling. Almost immediately the superior anterior wall of a cyst was exposed. The wall was exceedingly thin, relatively transparent and bluish and was described as "thin as tissue paper." The cyst wall was inadvertently punctured, and there was an immediate escape of a thin, pale, straw-colored, lymph-like fluid, previously seen in cases of typical hygroma. The incision was enlarged to allow a wide dissection. The cystic tumor was firmly adherent to the anterior border of the sternocleidomastoid muscle on the right and to the pretracheal muscles but not to the trachea. Consequently a portion of these muscles had to be included in the excision in order to be certain that the entire mass was extirpated. In other respects the tumor was readily liberated, there being no important structures immediately concerned. The wound was closed without drainage, fine interrupted silk sutures being used in the approximation of the platysma muscle, subcutaneous tissues and skin. The operative diagnosis of hygroma could be made from the gross appearance of the tumor.

Postoperative Course.—The patient convalesced normally; the wound healed per primam intentionem and the patient was discharged on March 29, six days after operation.

Gross Pathologic Examination.—The specimen, a cystic tumor from the neck, on section was seen to be trabeculated and multilocular. There were many larger cysts of varying size and numerous minute cystic cavities. There was one well defined lobule as large as a cherry. The walls of the cysts were frail and thin, and the lining was smooth and glistening. The contained fluid had the typical limpid, lymphlike appearance. Some muscle and adipose tissue were attached to the tumor.

Microscopic Examination.—Low Power: The section showed a large area of striated muscle adjoining a hygromatous cyst. The endothelial lining of the cyst appeared with a subendothelial zone of pink-staining, hyaline-appearing connective tissue. Below this, between this cyst lining and the muscle, was a wide area of hygromatous stroma of pink-staining, wavy, spongy appearance. This stroma contained relatively few nuclei and an abundance of small blood vessels and lymph spaces. The hygromatous stroma was seen penetrating into the planes between bundles of muscles. These penetrating bands of stroma were fibrillar in structure and contained elongated, flattened nuclei. There were wide areas of muscle fibers which showed poor affinity for stain and gave a glassy, hydropic appearance.

High Power: The cyst lining showed the usual type of endothelial cells, with elongated, flattened nuclei. The subendothelial zone was composed of fibers also supplied with elongated, flattened nuclei. The fibers of hygromatous stroma had a hyaline appearance. The neighboring muscle fibers showed a variability of appearance; in certain areas, the muscle fibers were swollen, hydropic and poorly stained; in other areas, longitudinally cut fibers showed rupture with transverse fracture, loss of striation and even fragmentation and degeneration to the point of solution. The hygromatous, fibrillar bands after penetrating between muscle bundles were seen to end by insinuating themselves in the form of minute fibrillar prolongations between the individual muscle fibers. The diagnosis was hygroma.

Follow-Up Note.—May 6, 1933: No answer to the questionnaire was received. The patient could not be traced.

CASE 12.—T. S., a housewife aged 42, was admitted to the Long Island College Hospital on Feb. 23, 1926, because of a swelling on the right side of her neck. She was discharged on March 6.

History.—She had had three children and two miscarriages. There was no history of serious illnesses. Six years previously, at the age of 36, the patient had

first noticed a slight swelling on the right side of the neck. This swelling had since gradually increased in size to that of an egg. It had never been painful or tender and had always been soft and fluctuant. There was no impairment of speech or deglutition.

Physical Examination.—The patient was a well developed, well nourished woman of middle age. General physical examination gave negative results. On the right side of the neck there was a swelling the size of a hen's egg, which protruded anterior to the sternocleidomastoid muscle in the upper part of the anterior triangle and extended downward to the lower border of the thyroid cartilage. It did not rise as the patient swallowed. The tumor was soft, smooth and fluctuant but not tender. There were no nodules to be felt in the swelling, and there was no redness of the overlying skin. The regional lymph nodes were not enlarged.

Clinical Examination.—The temperature was 99 F., the pulse rate 80 and the respiratory rate 20. The erythrocyte count was 4,420,000, the hemoglobin content 90 per cent and the leukocyte count 7,400. The specific gravity of the urine was 1.028. A faint trace of albumin was found. An occasional white blood cell was seen on microscopic examination.

The preoperative diagnosis lay between cystic hygroma and branchial cyst. The position of the tumor would have lent support to the diagnosis of cyst of branchial cleft origin; the consistency, however, favored the diagnosis of hygroma.

Operation.—The excision of the hygromatous tumor was performed on February 26. Nitrous oxide and ether were used. The mass was situated in the right anterior triangle. A transverse incision was made in the fold of the neck over the prominence of the tumor. A thin-walled cystic mass was exposed. During the dissection, a small opening was made in the wall of the cyst. Thereupon the hole was enlarged for the purpose of exploring the extent of the cyst with the finger. The cavity of the cystic mass was traversed by numerous trabeculae, which made digital examination impossible. By sharp and blunt dissection, the cystic tumor was liberated from the carotid sheath and the sternocleidomastoid muscle. The dissection was continued upward to the base of the skull and to the vicinity of the mastoid and styloid processes. The important structures of the neck, which were exposed during this procedure, were carefully spared. A full view was obtained of the digastric muscle, the hypoglossal nerve, the large vessels of the neck and the vagus nerve. The right thyroid lobe was exposed and found to be normal in gross appearance. Careful ligature of the numerous small vessels was done. The subcutaneous tissues and skin were closed with interrupted sutures of fine silk.

Postoperative Course.—The convalescence was uneventful. The wound healed without reaction or the accumulation of serum. The patient was discharged in good condition on March 6, eight days after the operation.

Gross Pathologic Examination.—The specimen was a tumor of the neck. After the escape of most of its contained fluid, it consisted of a mass of soft spongy tissue measuring 5 by 2.5 by 1 cm. On section of the mass, numerous cystic cavities lined by an endothelium-like membrane were seen. The fluid contents of the cysts were lymphlike. The cavities were devoid of anything resembling sebaceous material or epithelial débris, such as is seen in cysts of branchial cleft origin.

Microscopic Examination.—Many lymph sinuses and cystic spaces were seen to be enclosed in thin delicate walls lined by a single layer of flat endothelial-like cells. Another section showed a lymph gland with marked chronic interstitial changes. The diagnosis was hygroma with chronic lymphadenitis.

Follow-Up Note.—May 6, 1933: No answer to the questionnaire was received. The patient could not be traced.

PHENOMENA DUE TO MISDIRECTION OF REGENERATING FIBERS OF CRANIAL, SPINAL AND AUTONOMIC NERVES

CLINICAL OBSERVATIONS

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The contracture of the facial muscles and the tendency to mass movements of the face which so often follow Bell's palsy have attracted the attention of neurologists since the earliest times, and a great many theories have been offered to explain these phenomena. Sir William Gowers [1] was inclined to ascribe the mass movements to a change in the functional state of the nucleus, and Oppenheim, who evidently held similar views, spoke of "irritation" of the facial nucleus. In 1906 Lipschitz [2] offered a more satisfactory theory when he claimed that the mass movements were due to misdirection of regenerating nerve fibers. Spiller [3] pointed out in 1919 that the same explanation might be offered for facial contracture. Various writers have attempted to explain the syndrome of crocodile tears and the auriculotemporal syndrome on the basis of misdirection of regenerating nerve fibers, and certain phenomena which follow regeneration of the third nerve have been ascribed to the same factor. As regards the regeneration of the spinal nerves, however, little application has been made of this theory. Surgeons have indeed suggested that when sensibility and motility fail to return after suture of the nerve misdirection of fibers may be to blame and have emphasized the importance of preserving the internal pattern of the nerve bundles as far as possible. It was not until Stopford's [4] paper appeared in 1926, however, that any effort was made to apply

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1. Gowers, W.: The Movements of the Eyelids, Med.-Chir. Tr. London **62**:429, 1879.

2. Lipschitz, R.: Beiträge zur Lehre von Facialislähmung nebst Bemerkungen zur Frage der Nervenregeneration, Monatschr. f. Psychiat. u. Neurol. **20**:84, 1906.

3. Spiller, W. G.: Contracture Occurring in Partial Recovery from Paralysis of the Facial Nerve and Other Nerves, Arch. Neurol. & Psychiat. **1**:564 (May) 1919.

4. Stopford, J. S. B.: An Explanation of the Two-Stage Recovery of Sensation During Regeneration of a Peripheral Nerve, Brain **49**:372, 1926.

this theory to the dissociation of sensation which is often found during regeneration of peripheral nerves, and little or no mention is found in the medical literature of the possibility of motor anomalies developing on the same basis. Neurologists have not been unanimous in accepting this point of view, and some eminent authorities still incline to the theory that the mass movements of the face, for example, are due to physiologic alterations of the facial nucleus. It is evident that if the theory of misdirection of regenerating nerve fibers is correct, it must be capable of wider application than it has yet received. It is the purpose of this paper to show that numerous symptoms encountered in the regeneration of cranial, spinal and autonomic nerves may be most satisfactorily explained on this basis.

ANATOMIC ASPECTS OF REGENERATION OF NERVES

An extensive literature has been devoted to the subject of degeneration and regeneration of the peripheral nerves. Most of this deals with histologic investigations made on experimental animals, but enough work has been performed on man to justify the conclusion that the essential features of these processes are the same in man as in other mammals. The facts which are of clinical interest may be given briefly.

Within a short time after a peripheral nerve is severed, the distal segment begins to show degenerative changes throughout its entire length. The axis-cylinders become swollen and finally fragmented. The myelin sheaths also break up into lipoid droplets, and the nuclei of the sheath of Schwann multiply rapidly and eventually form protoplasmic bands. The proximal segment of the nerve also undergoes degeneration for a short distance from the wound, as far as the first node of Ranvier, it is claimed. Within a few hours after section, the distal ends of the axis-cylinders begin to proliferate, and soon a thick brush of fine neurofibrils begins to grow out from the terminal segment of the nerve trunk. It has been shown that from three to six of these fine fibers may arise from each of the severed axons. The newly formed fibers are not always correctly oriented, for some of them stray off laterally and others grow backward into the proximal stump. The degenerating fragments of the distal stump, however, seem to exert a definite attraction on the regenerating fibers, and many, if not most, of the new fibers penetrate the scar of the wound and enter the protoplasmic bands which the neurilemmal nuclei have formed. Within these bands, which Cajal terms "sheaths," the newly formed fibers follow the course of the degenerated nerve, even to its finest branches. It is important for our argument to point out that in cases in which there is no obstacle to regeneration the number of fibers in the regenerated nerve may eventually exceed the number present in the nerve before section. Moreover, it is quite clear from experimental work that the regenerating fibers

do not always follow the same course that they pursued before operation. In cases in which two adjacent nerves are sectioned, the fibers may even enter the wrong nerve. One of Cajal's experiments may be cited in this connection. He severed the sciatic nerve of a cat at a point where it is composed of two separate nerve trunks, the peroneal and the tibial. The regenerating fibers of the tibial nerve entered the distal stump of both the tibial and the peroneal nerve, and those arising in the proximal stump of the peroneal nerve entered both distal stumps in the same way. Cajal [5] stated:

> . . . those sprouts which reach the peripheral stump enter it in great disorder; some sheaths have no sprouts and the great majority, if not all of the sheaths, instead of receiving the outgrowth of the same axon which was present in them before the operation, are invaded by sprouts which have come from axons in other regions of the central stump. Thus, the observed facts compel us to reject the supposition of those authors who believe that the newly formed fiber infallibly ends in the old sheath of the peripheral stump and unerringly restores the old terminal arborization, thus preserving the anatomical and physiological individuality of the pre-existing conductor. On the contrary the errors and incongruences are so many that one wonders whether the whole mass of sprouts which penetrate into the peripheral stump is not entirely superfluous, seeing that the connections between central neurons and the peripheral structures which formed, since the embryonic period, such an intimate anatomical and dynamic whole, are now so disturbed and confused. Moreover, in cases of rapid nervous reunion after hemisection or complete sections with small scar, sensibility and movement are only more or less imperfectly restored.

It is universally admitted that certain changes occur in the nerve cells when their axons are divided. The cell becomes swollen, the nucleus is displaced and the Nissl substance and neurofibrils are broken up into fine granules. This process is termed the axon reaction. It seems to vary in intensity, depending on various factors such as the distance of the wound from the cell body and the severity of the trauma. It apparently is also more severe in certain nerves than in others. The process is a reversible one, and in cases in which the nerve ultimately regenerates most of the neurons so affected regain their original appearance and staining qualities. There is no evidence, of course, of any proliferation of nerve fibers in the spinal cord or in the posterior root ganglions in response to injury to their axons. In this connection Ramón Cajal [5] stated:

> Concerning the restoration of central connections, it would be still more satisfactory to admit the re-arrangement or reorganization of pyramidal and sensory-reflex collaterals destined to rectify the aberrations of connection that have occurred in the periphery. But the dogma of the irregenerability of the central paths prohibits us from putting forth such a hypothesis.

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5. Ramón y Cajal, S.: Degeneration and Regeneration of the Nervous System, New York, Oxford University Press, 1928.

It is evident, therefore, that Cajal's anatomic investigations reveal the constant occurrence of misdirection of regenerating nerve fibers into terminal segments of peripheral nerves formerly supplied by different fibers. It seems to be equally clear that there is no anatomic evidence to indicate that the central neurons can form new connections as a result of the changes they undergo when their axons are interrupted. Cajal expressed the belief that "disconnected or useless neurons" rapidly atrophy and disappear.

CRANIAL NERVES

The Seventh Nerve.—The distortion of facial movements which remains as a residuum after severe Bell's palsy is one of the commonest and most troublesome problems which confront the clinical neurologist. It

Fig. 1.—*A,* a patient with facial palsy and subsequent regeneration of the nerve. Note the facial contracture on the right side. *B,* the same patient, showing how on exposure of his teeth the right eyelid closed.

is usually termed "facial contracture." The condition may be illustrated by the typical case history which follows:

Mrs. G. G., a previously healthy woman of 25 years, went for a long drive in an open car in November 1928. The weather was cold, and she had no protection from the wind, which numbed her face and ears. That evening she was conscious of a dull pain in her right ear, and this persisted during the following day. On arising the next morning, that is, on the second day after the ride, the patient found that she could not close her right eye or move the right side of her mouth. There was complete paralysis of the right facial nerve when she was examined on the fourth day. Neurologic examination gave otherwise negative results. Medical and dental examinations and examination of the nose and throat also gave negative results. The Wassermann test was negative. When the right facial nerve was stimulated with electric current on the thirteenth day of the paralysis, no reaction to the faradic current could be elicited in either the nerve

or the muscles and the muscles reacted by a slow and "wormlike" contraction when the galvanic current was employed. A complete reaction of degeneration was present therefore. The only therapeutic measure employed was gentle massage, and no electrical treatment was given. Within a few days the facial muscles became much relaxed. The lower lid fell away from the bulb, and tears ran over and down the cheek. The right corner of the mouth sagged, and the nasolabial fold and the wrinkles on the forehead were abolished. There was no evidence of improvement until the middle of March 1929, when the tone of the right side of the face began to improve, and soon after this the patient noticed some return of power. She was examined again in May 1929. A striking change had occurred. Tone was greatly increased in the affected side of the face. The right nasolabial fold was much deeper than the left, the right palpebral fissure was smaller than the left and the folds and wrinkles of the forehead were deeper on the right than on the left. The patient could close the right eye, move the right side of the mouth and wrinkle the right side of the forehead. It was evident, therefore, that the nerve had regenerated and that all the muscles had received motor nerve fibers again. However, all movements were grossly distorted. On repeated tests it was evident that whenever the patient moved any part of the right side of the face every muscle supplied by the seventh nerve on that side contracted to some extent. For example, when she closed the eyelid, the mouth was drawn to the right. When she showed her teeth, the right eyelid was partially closed. The muscles of the forehead were involved in both movements. On close inspection it was observed that every few seconds the right side of the patient's mouth would twitch spontaneously. It was easily determined that the twitching of the mouth was an accompaniment of the natural blinking of the eyelids. The blinking was not associated with any other movement on the left side of the face but was accompanied by a slight twitch of all the facial muscles on the right side. It was only the movement of the mouth, however, which was obvious enough to attract the examiner's attention. The state of tone of the right side of the face was not always the same. At certain times it was intense, and the nasolabial fold was deep. Again the face was perfectly symmetrical. During conversation, tone was almost always much increased, and it seemed to be nearly normal when the patient was quiet. The patient was requested to lie down, therefore, and to try to relax as completely as possible. Under these circumstances, the face was symmetrical for several minutes at a time. Reactions to electrical stimuli were normal.

The patient was told that the nerve had regenerated but that the nerve fibers had been misdirected to muscles other than those they had originally supplied. She was advised to try to regain control of the facial movements by exercises before a mirror. From time to time she reported that she was carrying out the exercises faithfully. At times she fancied that there was some improvement. Finally, in June 1935, seven years after the onset, the patient was examined once more. All the phenomena described were still present. It is possible that there had been a little improvement, but it is certain that there was no material change. All the associated movements were quite evident. There was still no true contracture of the facial muscles, for when the patient was relaxed the face was still symmetrical.

This case is not an exceptional one in any sense, and it would be easy to discover at least a hundred similar cases in our records. In our experience some evidence of mass movement and "facial contracture" is

invariably present in every case in which the facial nerve degenerates and subsequently regenerates. These phenomena are inevitable, therefore, in all severe facial palsies of long duration, except in those rare instances in which the nerve fails to regenerate. On the other hand, one never observes sequelae of this type in the transient facial palsies which are not associated with changes in the reactions to electrical stimuli and which disappear within a few days or weeks. It is impossible for us to attribute these phenomena to "irritation" of the nucleus, for they persist without definite diminution throughout the rest of the patient's life. Irritative phenomena, as a rule, vary in intensity from time to time, but the mass movements and "contracture" are always exactly the same when they have once become fully established. They are invariably associated, and we have never seen one without the other. Every innervation of the face, whether it is volitional or emotional, activates every muscle supplied by the facial nerve. Thus, for example, when the patient closes the eyelid, the muscles about the mouth and those of the forehead also contract. Evidently the neurons which formerly sent impulses only to the eyelid are now connected with all the facial muscles. The multiplication of the regenerating nerve fibers and their tendency to grow into all parts of the degenerated nerve trunk have resulted in fibers from each part of the facial nucleus becoming diffusely distributed throughout the facial musculature. The so-called contracture is most logically explained, as Spiller [3] has indicated, on the same basis. Since any given group of facial muscles receives stimuli originally intended for any one of the other groups, each group must receive as many stimuli as all the facial muscles together under normal conditions. Consequently, the tone of the muscles is greatly increased so long as the facial muscles are receiving motor impulses. This is not a true contracture, i. e., the muscles are not anatomically shortened, for when the patient is relaxed it disappears completely. The "contracture" is most pronounced when the patient is under emotional stress or is engaged in animated conversation, indicating that it is due to diffusion of the numerous stimuli which play on the facial muscles under such circumstances.

Howe and Tower [6] have shown by experimental means that as a result of the multiplication of regenerating neurofibrils a single axon may eventually supply two or more muscles. Stimulation of one of these muscles, therefore, will always result in contraction of the other one, even if the facial nerve has been severed from the brain stem. In a few cases it is possible to demonstrate this phenomenon in patients.

6. Howe, H. A.; Tower, S. S., and Duel, A. B.: Facial Tic in Relation to Injury of the Facial Nerve: An Experimental Study, Arch. Neurol. & Psychiat. **38**:1190 (Dec.) 1937.

For example, in a young woman recently examined who exhibited fully developed mass movements of the face following facial palsy, stimulation of the lower lip with a weak faradic current always resulted in contraction of a small group of muscle fibers above the eyebrow. Conversely, stimulation of the muscles above the eyebrow caused a flicker of the lower lip. The muscles of the eyelid and upper lip did not contract, showing that the current was not strong enough to spread over the face and cause this phenomenon by diffusion.

One might naturally inquire at this point why phenomena indicative of misdirection of regenerating nerve fibers are so obvious and so common in facial palsy and so inconspicuous in palsy of other peripheral nerves. The answer is to be found in the frequency of facial palsy and in the peculiar physiology of the facial nerve. It is probable that the facial nerve is paralyzed more often than any other nerve in the body. In a large percentage of cases it degenerates, and almost invariably more or less complete regeneration occurs. Facial palsy is usually a harmless condition, and the patient therefore survives. The face is so distorted that the patient almost invariably returns for further treatment in the vain hope of relief. The movements of the face are of extraordinary delicacy and of great importance in social life. The least change in facial movement or in tone of the facial muscles attracts attention at once. One reads faces so constantly that slight changes are recognized as changes in expression, even when one cannot analyze them as contractions of definite muscles. The significance of the movement is recognized without the movement itself being observed. The muscles about the eyelids are especially important in this regard, and the chief anatomic basis for changes in expression of "the eyes" is probably to be found in minute changes in the tone of these muscles. The least alteration of facial innervation, therefore, inevitably attracts one's attention.

It must be pointed out in this connection that the mass movements of the face and "facial contracture" occur in all cases in which the facial nerve degenerates and subsequently regenerates. They may be just as intense in cases in which the nerve has been paralyzed spontaneously, i. e., in cases of common Bell's palsy, as in cases in which the nerve has been sectioned and sutured. The anatomic basis of Bell's palsy is, of course, unknown, but it does not seem likely that the lesion can be such as to sever the nerve completely and destroy the relations of the various fiber bundles in the nerve in any gross anatomic sense. This observation, therefore, suggests that phenomena due to misdirection of regenerating fibers may be found in the peripheral nerves when the lesion is such as to leave the intrinsic nerve pattern intact.

The Third Nerve.—The third nerve supplies the levator palpebrae, the internal rectus, the superior rectus, the inferior rectus, the inferior

oblique and the constrictor muscles of the pupil. One would, therefore, expect to find motor anomalies due to misdirection of nerve fibers in cases in which the nerve has been severely injured and has subsequently regenerated. An instance of this nature may be given for illustration.

J. W., a race horse trainer, who had always been healthy, was struck on the head in an automobile accident in 1929, when he was 38 years of age. He was unconscious for many hours, and when he regained consciousness it was found that there were complete ophthalmoplegia externa and interna on the right side. There was also partial loss of vision in the right eye. These symptoms were due to fracture of the base of the skull with laceration of the nerves near the sphenoid fissure, for there was a depressed fracture in the right frontal region which extended into the posterior part of the orbit. The patient noticed no change in the condition of the eye until several months later, when the lid began to open a bit and the eye became adducted.

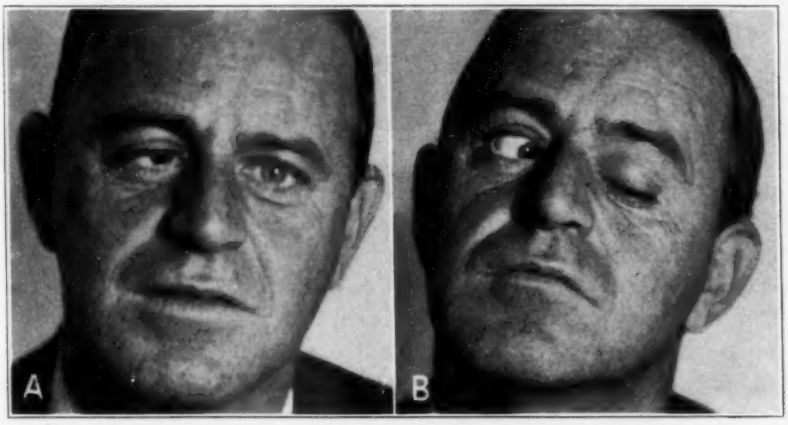

Fig. 2.—*A*, a patient with palsy of the third nerve and subsequent regeneration of the nerve. Note the adduction of the right eye, the drooping lid and the dilated pupil. *B*, the same patient attempting to look down and to the left. The right eye is adducted but not rotated downward, and the lid is elevated.

Examination in October 1936, seven years after the injury, revealed that the right eye was strongly adducted, the right pupil was dilated and the right lid drooped. This condition is shown in figure 2 *A*. It was possible to adduct the right eye fully, but abduction beyond the midline was impossible. In the same way, attempts to move the eye upward and downward resulted in little or no movement in the desired direction, but the bulb was always adducted and the lid elevated. Indeed, some elevation of the lid occurred when the patient adducted the eye voluntarily. If he tried to look downward when the lids were closed, there was a strong tendency for the lid to snap open, showing that the elevation of the lid was the result of an active contraction of the levator muscle and not merely a failure of this muscle to relax. No change could be induced in the pupil by any means.

Bielschowsky [7] cited several cases similar to this one, and Bender [8] described an interesting case of the same type. In all of these cases there are features which frequently recur: 1. Certain movements of the bulb are absent. 2. The eye is frequently adducted when the patient attempts to perform some other movement. 3. The lid is elevated when the patient attempts to look downward or inward just as it is when he tries to look up. Bielschowsky and Bender agreed that these phenomena are probably due to misdirection of regenerating nerve fibers which arrive at muscles to which they do not belong. Bielschowsky suggested that the tendency for elevation of the lid to result from the impulse for adduction or downward rotation is due to the fact that the regenerating fibers prefer certain "routes" for growing in the wrong sheaths. We doubt that the regenerating nerve fibers follow any special route and wish to offer a somewhat different explanation for the phenomena described. Suppose that during the course of regeneration of the third nerve every muscle supplied by this nerve receives an abundant supply of neurons but that each muscle receives some of the fibers which formerly supplied every other muscle. Every effort to perform a movement in which the third nerve normally functions will therefore result in contraction of every muscle which receives its innervation from the third nerve. The attempt to look downward will cause contraction of the inferior rectus and of the superior oblique. No movement can take place in the vertical plane, however, for the superior rectus and the inferior oblique also contract at the same time. The internal rectus contracts with the other muscles, and since this is not opposed by any special action of the external rectus, the eye will be adducted. The lid will be lifted at the same time, for the levator has received some of the fibers which formerly innervated the superior oblique or the inferior rectus. When the attempt is made to look inward or upward, the same movements occur, for the same muscles contract, with the exception of the superior oblique. Abduction of the eye should occur normally if the sixth nerve is not involved. In this hypothetic case, therefore, we appear to find all the phenomena mentioned previously which seem to require explanation. It is likely that the loss of some movements of the eye in these cases may be due to simultaneous contraction of opposing groups of muscles rather than to failure of adequate regeneration. The tendency of the eye to be adducted when other movements are attempted may be due to the fact that the action of the internal rectus is not opposed by synchronous

7. Bielschowsky, A.: Lectures on Motor Anomalies of the Eyes: Paralysis of Individual Eye Muscles, Arch. Ophth. **13**:33 (Jan.) 1935.

8. Bender, M.: The Nerve Supply to the Orbicularis Muscle and the Physiology of the Movements of the Upper Eyelid, with Particular Reference to the Pseudo-Graefe Phenomenon, Arch. Ophth. **15**:21 (Jan.) 1936.

contraction of the external rectus. In the same way the elevation of the eyelid in association with the impulse for adduction may be explained by the supposition that the levator has received nerve fibers which formerly supplied the internal rectus. It is, of course, obvious that in many cases in which these phenomena are found incomplete regeneration of the third nerve may complicate the picture.

SPINAL NERVES

The Ulnar Nerve.—A typical instance of section and suture of the ulnar nerve with excellent regeneration is found in the following case:

C. E., a young mill worker, cut his left wrist with a piece of glass on June 26, 1932. Operation was performed the following day. The ulnar nerve was found to be completely severed and was carefully sutured end to end. The ulnar artery and all the tendons on the ulnar side of the flexor surface of the wrist were also severed. The tendons were sutured and functioned normally afterward, so that the injury to the tendons played no part in the subsequent symptoms. The circulation was always adequate. After operation there was a slight infection, which persisted for months and finally disappeared only after some silk sutures were discharged from the wound. There was, of course, complete loss of function of the ulnar nerve from the moment of the accident.

About eight weeks after the operation the patient began to notice improvement in sensibility in the anesthetic area, and shortly after this there was some return of motor power. This improvement slowly progressed, and within a year he regarded the hand as being almost completely restored. His work demanded strength rather than coordination, and his hand functioned satisfactorily in this regard. He admitted on close questioning, however, that he could not fasten buttons with his left hand.

Examination on Feb. 19, 1937, revealed that there was little or no wasting of the muscles of the affected hand. Strength in the muscles supplied by the ulnar nerve was excellent and compared favorably with that of the same muscles of the right hand. There was no evident disturbance of the circulation, and the skin and the nails were normal. The thresholds of tactile sensibility, thermal sensibility and pain were identical with those found on the corresponding points of the right hand. Tests for tactile sensibility were done with fine wisps of cotton wool, for pain sensibility with a weighted needle and for thermal sensibility with tubes of measured temperature. However, there was a gross deficiency in certain forms of sensibility. Over the little finger tactile localization was greatly reduced, and the patient could not recognize the aspect or the segment to which the stimulus was applied. He was not always sure of the finger touched. Two point sense (compass test) was quite absent over the tip of the little finger. Sense of passive movement of the terminal joint of the little finger was greatly reduced, but this was not true of the proximal and middle joints or of the ring finger. Strong pricking, scratching or scraping of the previously anesthetic area caused a widespread tingling feeling over the whole area. This reaction was minimal, however, when light touch with a fine wisp of cotton was applied. The motor functions were definitely altered. When the patient adducted the thumb strongly, the interosseus muscles all contracted involuntarily. The little finger was always strongly abducted, and the ring finger was adducted with its middle interphalangeal joint hyperextended. Conversely, whenever these muscles were innervated, the

thumb was always strongly adducted. This movement of the thumb might be somewhat inhibited by the contraction of the antagonists, but the muscle could always be felt to contract. Careful palpation revealed that when any of the intrinsic muscles supplied by the ulnar nerve were innervated, all of these muscles contracted to some extent. The muscles of the forearm which were never paralyzed did not take part in these abnormal movements.

The Median Nerve.—The following case history may be offered to illustrate the phenomena sometimes found in regeneration of the median nerve:

R. S., a young physician, received an injury in February 1932 which severed the left median nerve at the wrist. The nerve did not regenerate well, and a neuroma formed at the site of the lesion. In December 1933 the neuroma was removed by Dr. Dean Lewis, and the nerve was sutured. For a time there was complete loss of function with anesthesia of the usual distribution. Within two months, however, sensibility and motility began to return, although up to the time this report was written normal function had not been regained.

Examination on Nov. 3, 1936, revealed the following findings: 1. The left thenar eminence was smaller than the right, and the tip of the index finger was somewhat atrophic. 2. All the muscles of the hand supplied by the median nerve contracted to some extent, although their strength as well as their bulk was diminished. The muscles of the forearm were not affected in any way. 3. When the patient flexed or opposed the thumb, there was always definite abduction of the index finger and flexion at the proximal joint. At the same time the tendons of the long flexors grew tense. This we attributed to contraction of the lumbricalis muscle, which may cause abduction and flexion of the proximal joint and may also cause traction on the tendon of the flexor profundus digitorum. Conversely, strong flexion of the index finger was always associated with contraction of the muscles of the thenar eminence. 4. Tests with fine wisps of cotton revealed tactile sensibility to be intact. The threshold was no higher in the affected fingers than in the corresponding areas on the right hand. Warm and cool tubes of measured temperature were appreciated equally well on the two sides. The threshold for pain, tested with a weighted needle, was exactly the same for the two hands. 5. Tactile localization was grossly impaired when the test was made with a wisp of cotton wool. The most the patient could do was to guess which finger was touched. He was not always sure of the finger and could never recognize which joint or aspect of the finger was touched. On the right side he never failed to recognize the segment and aspect of the finger touched. When firmer pressure was made, the answers were more nearly correct. 6. Two point sense was greatly diminished, for the patient could not distinguish between one point and two when the tips of the compass were separated by 1 cm. and applied to the tips of the first and second fingers; whereas on the right, he made no errors when the tips of the compass were separated by 3 mm. The loss of two point sense was almost complete when light pressure was made and was less evident when the tips of the compass were applied firmly. 7. Stereognosis was much impaired on the left. Small letters carved from blocks of wood were employed. The patient was required to feel these with the first two fingers and the thumb. With the fingers of the right hand he recognized them instantly. With the fingers of the left hand he was unable to do more than guess and made about 50 per cent errors. He was able to guess correctly by running a finger over the outlines of the letter. 8. Pricking with a pin in the affected area caused a diffuse sensation of a peculiar nature over the entire zone of altered sensation. The same effect was produced

by scraping and scratching. Light touch caused a mild degree of this reaction, which was most pronounced when strong stimuli were employed. 9. Heat was sometimes felt as cold or pain, and a pinprick was sometimes felt as heat. Even light touch would at times cause a feeling resembling that of a pinprick.

Comment.—It is not necessary to discuss in detail the motor anomalies in these cases, for they are obviously identical with the more conspicuous disturbances of facial innervation described previously.

As regards the sensory phenomena, we wish to emphasize several points: (1) the complete return of tactile sensibility and of appreciation of slight differences in temperature; (2) the failure of tactile localization, two point sense (compass test) and stereognosis to return to approximately normal levels; (3) the tendency for strong sensory stimuli to cause diffuse sensations, and (4) the perversions of sensibility, such as the painful reactions to gentle scraping and of cold feelings when heat is first applied.

The return of normal tactile and thermal sensibilities without corresponding improvement in tactile localization, two point sense and stereognosis is not an isolated or mistaken observation, for it has been reported by a number of other writers. In Henry Head's [9] case reports dealing with the return of sensibility in cases of complete section of the medial and ulnar nerves, one frequently finds that tactile and thermal sensibilities were completely restored but that the compass test (two point sense) was still imperfectly appreciated. This same result was observed in Head's famous experiment on his own arm. Stopford [4] made the same observations and offered the following explanation:

1. That heterogenous connections within certain limits may be succeeded by recovery of all-or-nothing response to pain, hot, and cold stimuli. The adequate stimulus is dependent upon the type and condition of the end-organ, whilst the change in consciousness depends upon the central connections. Pain, heat, and cold fibers reaching homogenous end-organs in any part of the sensory field under investigation will function as soon as connections from end-organ to thalamus are reformed in their full continuity.

2. That heterogenous connections in the case of fibers concerned with the higher aspects of sensation are not likely to be succeeded by any return of sensibility, either immediate or in the future. Fibers concerned with the higher aspects of sensation, such as spatial recognition in one, two, or three dimensions, may reach homogenous end-organs without any recovery of function that can be discovered even by graduated tests, but it seems possible under these circumstances that by re-education some recovery may follow at a later date. The extent of recovery under such conditions not only depends upon fortuitous regeneration but also upon the educability of the patient.

If we may be permitted to attempt to simplify these statements, we may say that Stopford pointed out that as soon as fibers conveying

9. Head, H.: Studies in Neurology, New York, Oxford University Press, 1920, vol. 1.

sensations of pain, heat and cold form connections with their proper end-organs, they will begin to function. On the other hand, regeneration of fibers concerned with tactile localization, two point sense and stereognosis will not lead to recovery, even if they chance to reach appropriate end-organs, because they will rarely if ever reach the same end-organs which they formerly supplied, and hence their function, which demands exact localization of stimuli, will not be restored.

The strange diffuse sensation which is characteristic of returning sensibility deserves some discussion. If one stimulates area A in a previously anesthetic area, one may well stimulate several neurons which formerly supplied areas B, C and D. The resulting sensations will naturally be referred to areas B, C and D, and the patient will experience feelings suggestive of multiple stimuli applied over a broad area. Strong stimuli, which may well be expected to stimulate several neurons, will cause such diffuse sensations, when touch with a single hair, which could scarcely stimulate more than one or two neurons, will not do so.

Stopford also offered an interesting explanation for the various perversions of sensibility sometimes found on examination of a patient during regeneration of peripheral nerves. If, for example, a burning sensation results when the patient is pricked by a pin, one may suspect that the stimulus has excited a "heat" fiber which has formed connections with a "pain" receptor. In the same way, the painful reaction to light touch or to scraping, which is sometimes observed, may be regarded as indicating that "pain" fibers have become connected with tactile receptors.

A number of authors speak of reeducation of the patient as if it were quite clear that it is possible for the patient to compensate in some way for the misdirection of peripheral nerve fibers. We are not convinced that this is possible. Certainly in the case of the facial nerve the mass movements and "facial contracture" are present throughout the rest of the patient's life without perceptible change. Head's famous experiment in which a nerve of his own forearm was sectioned and carefully sutured at once would seem to indicate that the power of reeducation in sensory nerves is negligible. Head stated: "But even at the end of five years after the operation, many errors of this kind are still present when the compasses are applied, even at a distance of 8 cm. over the abnormal area of the forearm." Head had made careful studies of sensibility in his arm during these five years, and if it were possible to reeducate oneself so as to compensate for such a defect in sensibility, one would imagine that he would have done so.

We wish to digress at this point to make a few remarks about the implications of the preceding statements as regards Head's theory of a dual system of sensory neurons. It is well known that he found in his experiments that cutaneous sensibility returns in two distinct stages

during regeneration of a peripheral nerve. First, pain and extremes of temperature are appreciated and then, after an interval, light touch, mild differences in temperature, tactile localization and two point sense. He claimed that this dissociation is due to the fact that there are two types of sensory neurons, one of which conveys crude sensation and regenerates rapidly and the other of which conveys the higher modalities of sensation and regenerates more slowly and less perfectly. The former he termed protopathic and the latter, epicritic. This hypothesis was criticized severely by Boring,[10] Trotter and Davies[11] and Cobb.[12] In general, these investigators concluded that there was no satisfactory evidence of the existence of a dual system of sensory neurons and that the return of sensibility was really a continuous process. Cobb stated:

> Dissociations of sensation due to peripheral nerve lesions arise from comparing stimuli not only qualitatively different but quantitatively unequivalent. In short, they are artefacts.

Further objections were raised by Pollock, who showed that the early return of pain sense in the intermediate zone, which Head attributed to regeneration of protopathic fibers, is really due to the assumption of function by adjacent nerves.

Stopford, however, supported Head's hypothesis. He rejected the theory that the protopathic and epicritic neurons regenerate at different rates, for he stated that the anatomic evidence is strongly against this possibility. He explained the delayed or incomplete return of epicritic sensibility by the theory of misdirection of nerve fibers, as we have mentioned previously. This theory offers an excellent explanation for the incomplete recovery of tactile localization and two point sense but does not throw any light on the delay in the return of appreciation of light touch and of slight differences in temperature, for fibers conveying sensations of warmth and coolness might be expected to function just as well when misdirected as those conveying feelings of heat and cold. In our opinion, the explanation advanced by Stopford does not offer any support to Head's hypothesis of a dual system of sensory neurons. If one discards the theory that the two groups of neurons regenerate at different rates, as Stopford does, one is left without any explanation for the phenomena Head described. We are inclined to ally ourselves with Cobb, Boring and Pollock in regarding the apparent dissociation of sensibility as an artefact and in rejecting the theory of a dual system of sensory neurons. It is quite conceivable that a tactile nerve fiber,

10. Boring, E. G.: Cutaneous Sensation After Nerve Division, Quart. J. Exper. Physiol. **10**:1, 1916.

11. Trotter, W., and Davies, H. M.: Experimental Studies in the Innervation of the Skin, J. Physiol. **38**:134, 1908-1909.

12. Cobb, S.: Cutaneous Sensibility in Cases of Peripheral Nerve Injury: Epicritic and Protopathic Hypothesis of Head Untenable, Arch. Neurol. & Psychiat. **2**:505 (Nov.) 1919.

for example, which during the process of regeneration had reached some area of skin other than that it originally supplied, might function well as regards tactile sensibility but might at the same time have no value in those forms of sensibility depending on exact localization of stimuli. In our opinion the most striking dissociation of sensibility which is observed in the course of regeneration of peripheral nerves is not between protopathic and epicritic sensibility but is between all degrees of tactile, thermal and pain sensibility, which always return if the nerve regenerates satisfactorily, and tactile localization, two point sense and stereognosis, which do not return to even an approximately normal level. We believe that this type of dissociation is due to misdirection of sensory nerve fibers.

AUTONOMIC NERVES

The Syndrome of Crocodile Tears.—The commonest example of misdirection of regenerating autonomic nerve fibers is seen in the so-called syndrome of crocodile tears, which is not a rare sequel of a certain type of facial palsy. We may illustrate this condition by giving in abstract the history in a typical case.

J. McN., a healthy man of 68 years, had a severe pain in his left ear in May 1932. The next day he suddenly found that he could not close his left eye and could not move the left side of his mouth. His ear was inflamed, and there was some discharge from the external canal. The pain continued, and his family physician who had been treating him became alarmed and sent him to the hospital on the tenth day of the paralysis. Examination revealed complete paralysis of the left seventh nerve, with striking loss of tone of the facial muscles. The left eye was not obviously dry, but there was no overflow of tears despite the relaxation of the lower lid. There was an intense herpetic eruption in the concha and external canal of the left ear. Stimulation with an electric current resulted in the typical reaction of degeneration. The patient was not reexamined until September 1933. He then stated that he had not recovered movement in the left side of the face until at least ten months after the paralysis. At about the time power of movement returned in his face, he began to notice that every time he took food into his mouth tears would run from his left eye and down his cheek. Even the smell of food would make his eye grow somewhat moist. He never noticed excessive tear secretion under any other circumstances. This reaction never failed to occur when he was eating, and he was inclined to believe that it was more pronounced when he was eating food with a strong flavor. Examination revealed the associated movements and increased tone which have been described previously in cases of regeneration of the facial nerve. Lacrimation was easily produced by giving the patient chewing gum. The tears were visible within a few seconds after he began to chew, and within a minute they were running down his cheek.

The syndrome of crocodile tears may occur in several forms. The only type which is not excessively rare is that associated with facial paralysis. It must be pointed out that this syndrome does not occur in

the common Bell's palsy, for the lesion in such cases is distal to the geniculate ganglion. The syndrome of crocodile tears occurs only when the lesion is in the geniculate ganglion or proximal to the ganglion. We have seen it in several cases of neurosyphilis in which the lesion is probably in that segment of the nerve which lies within the subarachnoid space, in one case of vascular disease associated with subarachnoid hemorrhage, in one case in which the facial nerve was injured during operation on the eighth nerve for Ménière's syndrome and in three cases of facial palsy associated with herpes zoster of the ear. This condition has been attributed by Ramsy Hunt to zoster of the geniculate ganglion.

Fig. 3.—A patient with the syndrome of crocodile tears. Note the contracture of the right side of the face and the tears running out of the eye. She has just eaten part of an apple.

The Auriculotemporal Syndrome.—This rare condition is a sequel of penetrating wounds, suppuration and surgical incisions in the region of the parotid gland which sever the auriculotemporal nerve. Immediately after the wound is made, an area of anesthesia is found over the temple in the region which this nerve supplies. Some months later, after the nerve has regenerated, a series of interesting phenomena appear whenever the patient takes food into the mouth. The area of skin which was formerly anesthetic becomes bright red and is covered with droplets of sweat, which may be so numerous as to cause the sweat to drip down over the cheek. At other times, that is, when the patient

is not eating, this area of skin is indistinguishable from the normal skin. One of us[13] has offered the following explanation for these phenomena:

> The auriculotemporal nerve contains afferent fibers conveying sensory impulses from the skin, vasodilator fibers destined for the subcutaneous arterioles and secretory fibers for the sweat glands which are derived from the cervical sympathetic system. For a short distance near the parotid gland the nerve is accompanied by secretory and vasodilator fibers which supply the parotid gland and are derived from the ninth nerve by way of the otic ganglion. . . . It is evident, therefore, that when the nerve is injured between the parotid gland and the point at which it receives its communication from the ninth nerve the various groups of nerve fibers enumerated may be severed and, in the process of regeneration, may become misdirected along pathways other than those they originally pursued. It seems probable that the auriculotemporal syndrome is the result of misdirection of some of the secretory fibers of the parotid gland so that they form connections with the sweat glands and blood vessels of the skin. As a result, when the patient is eating and a volley of nervous impulses passes over the parotid fibers, paroxysmal sweating and vasodilatation occur in the distribution of the auriculotemporal nerve.

SUMMARY

We have attempted to show that various disorders of motility and sensibility which appear in the course of regeneration of the cranial, spinal and autonomic nerves are most easily explained by the assumption that the regenerating axons have gone astray and have formed peripheral connections other than those they originally possessed. This hypothesis is strongly supported by anatomic studies of regeneration which seem to show that regenerating nerve fibers rarely follow the course they formerly pursued. The mass movements of the face following facial palsy and similar disorders of ocular movements following palsy of the third nerve are cited in this connection. Several cases of lesions of the spinal nerves are described in which there were phenomena attributable to misdirection of the regenerating nerves. The auriculotemporal syndrome and the syndrome of crocodile tears are given as illustrations of misdirection of autonomic nerve fibers.

Dr. Frank Walsh supplied the illustrations.

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13. Ford, F. R.: Paroxysmal Lacrimation During Eating as a Sequel of Facial Palsy (Syndrome of Crocodile Tears), Arch. Neurol. & Psychiat. **29**:1279 (June) 1933.

HEMORRHAGIC INFARCTION OF THE GREATER OMENTUM

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In recent years interest in abdominal visceral infarction has been reawakened.[1] Much of the literature, however, has been concerned with mesenteric vascular occlusion and its effect on the gastro-intestinal tract.[2] The purpose of the present communication is to record a case of thrombosis of the omental venous system not associated with venous thrombosis elsewhere in the abdomen or with torsion of the omentum.

REPORT OF A CASE

History.—C. F., a 53 year old white man, entered the Bellevue Hospital on June 3, 1936, because of dyspnea, orthopnea and swelling of the ankles. Since 1929, when a 4 plus Wassermann reaction of the blood was discovered, he had received intensive antisyphilitic therapy. A diagnosis of arteriosclerotic, hypertensive syphilitic cardiac disease was made in 1934, when the patient was first seen, suffering from cardiac failure. Except for moderate diminution of cardiac reserve and occasional attacks of severe precordial pain, he felt well until late in May 1936, when symptoms of congestive failure recurred gradually.

Examination.—Physical examination on admission revealed an obese, orthopneic and cyanotic white man. The pupils were irregular and reacted sluggishly to light and in accommodation. The veins in the neck were distended. The heart was enlarged, and its sounds were of poor quality, the pulmonic second sound being greater than the aortic second sound. The rhythm was regular, with an apical gallop. There were no murmurs. The systolic blood pressure was 150 mm. of mercury, and the diastolic pressure, 118 mm. Râles were heard at the base of each lung. The abdomen was soft and not distended, and there was no free fluid. No masses or viscera were palpable. The external hernial rings were normal. Pretibial and sacral edema were marked. Neurologic examination gave negative results.

The temperature was 101.6 F. and the pulse rate 110. Examination of the blood revealed 4,500,000 red cells, with 74 per cent hemoglobin, and 12,050 white cells, with 80 per cent polymorphonuclear leukocytes. The urine contained albumin

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1. Connor, Lewis A.: A Discussion of the Role of Arterial Thrombosis in the Visceral Diseases of Middle Life Based upon Analogies Drawn from Coronary Thrombosis, Tr. A. Am. Physicians **47**:67, 1932.

2. Lazarus, Joseph A.: Mesenteric Vascular Occlusion, Am. J. Surg. **33**:129, 1936. Boyce, F. F., and McFetridge, E. M.: Mesenteric Vascular Occlusion, Internat. S. Digest **20**:67, 1935. Robey, William H.: Thrombosis in Abdominal Viscera, M. Clin. North America **16**:845, 1935.

(3 plus). The Wassermann reaction of the blood was negative. The electrocardiogram revealed sinus tachycardia, left bundle branch block, a deep Q_1 deflection and an inverted T_1 deflection.

Course.—The next day the patient appeared worse and complained of a severe sticking pain in the left upper quadrant of the abdomen. The pain was never colicky and was not associated with nausea or diarrhea. The abdomen was not distended or rigid. There was exquisite hyperesthesia of the skin over the left half of the abdomen, especially the upper quadrant. Deep pressure did not increase the pain, and there was no rebound tenderness. No viscera or masses were palpable, and the hernial rings were normal. Enemas gave normal returns. The temperature was 103 F., and the white cell count was 14,300, with 87 per cent polymorphonuclear leukocytes. On the second day after the patient's admission the same findings were noted by the surgical consultant. The white cell count had risen to 23,500, with 92 per cent polymorphonuclear leukocytes. The patient became comatose and died forty-eight hours after admission. The final clinical diagnoses were: arteriosclerosis, hypertension and syphilis; enlargement of the heart, coronary sclerosis and coronary ostial stenosis with myocardial infarction; sinus tachycardia; cardiac insufficiency, as demonstrated by marked physical signs, even when the patient was at rest, and splenic infarction.

Postmortem Examination.—Autopsy was performed three hours after death. On section, the parietal peritoneum was smooth and glistening, and there was no free fluid. The viscera occupied their normal positions, and there were no hernias. The greater omentum, which measured 15 by 23 cm. and contained abundant fat, was free and showed no torsion or adhesion to any of the viscera. The left third of this structure was outlined sharply by its deep purple, lusterless appearance. This portion was thickened, firm and inelastic. On the posterior aspect, about 8 cm. from the attached end, a large branch of the left gastro-epiploic vein was completely occluded by a red thrombotic mass, which was adherent to the wall of the vein. Propagated thrombi were present in the smaller veins in the immediate vicinity. The walls of the veins showed no significant macroscopic changes. The arteries of the omentum were normal. Except for atherosclerosis of the abdominal aorta, the remainder of the abdominal vascular system was normal.

The gastro-intestinal tract and the mesentery were normal. The liver and spleen showed chronic passive congestion, the latter showing, in addition, a small organized infarct. The heart was tremendously enlarged, and there was a large healed infarct in the left ventricle and the interventricular septum. A mural thrombus, organized at its base but friable at its periphery, overlaid the infarct. All the coronary arteries were sclerotic, and the anterior descending branch of the left coronary artery was closed by an organized canalized thrombus. There was moderate aortic atherosclerosis. The lungs were edematous and contained patches of lobular pneumonia.

Microscopic study of sections through the omentum revealed extensive hemorrhagic infarction, with necrosis of the omental tissue. Almost all the veins were occluded by thrombi, composed chiefly of platelet columns with marginated leukocytes and conglutinated red blood cells. No significant lesions of the walls of the veins were observed. The omental arterial system was normal.

COMMENT

This case is interesting from the pathologic as well as from the clinical standpoint. The facts that the occluded omental vessels were veins, that the corresponding arteries were patent and that there was

absence of any abnormal omental arteriovenous communications preclude the possibility that this lesion was the result of emboli from the mural cardiac thrombus.

Venous thrombosis is well known in cases of torsion of the omentum (Jeffries [3]). Such torsion may be primary (idiopathic) or secondary to hernia or some other intra-abdominal change. However, in this case no evidence of torsion was demonstrated at autopsy. Transient torsion during life cannot be excluded but in view of the fact that the patient was in bed because of cardiac failure this idea does not merit serious consideration.

Reference to only one other instance of extensive hemorrhagic infarction of the omentum was found in the literature. Hines [4] reported a case in which a white man of 54 complained of abdominal pain of two weeks' duration. Physical examination gave negative results except for a tender mass in the left upper abdominal quadrant. At operation, multiple omental venous thrombi were found, but exploration revealed no other changes. The patient died of peritonitis, and at autopsy the portal, superior mesenteric and splenic veins were found to be thrombosed, with hemorrhagic infarction of the greater omentum. The other abdominal viscera were normal. The present case differed from that reported by Hines in that the infarct was the result of omental venous thrombosis without involvement of the portal system.

The interpretation of the abdominal pain in this case presented some difficulty. A presumptive diagnosis was made of splenic infarct following emboli from a cardiac thrombus. The differentiation between splenic and omental infarction is almost impossible and depends perhaps on the accurate location of a palpable mass. No such clue was available in this case. Infarcts of the kidney can be suspected if there is hematuria; those of the gastro-intestinal tract, if there is vomiting, melena or intestinal obstruction.

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3. Jeffries, John W.: Torsion of the Great Omentum, Ann. Surg. **93**:761, 1931.

4. Hines, Lawrence W.: Hemorrhagic Infarction of the Greater Omentum, Illinois M. J. **66**:166, 1934.

EFFECT OF HYPOPROTEINEMIA ON WOUND DISRUPTION

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AND

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The rupture of abdominal wounds, with or without evisceration, is an old story. Even with the development of modern aseptic technic and a more intelligent handling of tissues, this complication continues to occur in from 1 to 3 per cent of all abdominal operations. Starr and Nason [1] found it in 0.61 per cent of their cases after laparotomy. Fincke [2] reported an incidence of 1.1 per cent; Meleney and Howes,[3] of from 1 to 2 per cent, and Eliason and McLaughlin,[4] of 0.27 per cent. Sokolov [5] reported an incidence in Europe of from 2 to 3 per cent. That this complication occurred in wounds which were not infected, in which hemostasis was good, in which trauma to the tissues and tension were minimal and in which unusual strain was obviated suggested that additional factors of a general character might be playing a part in the disruption of certain abdominal wounds. The fact that the majority of these accidents occur after operations on the upper part of the gastro-intestinal tract or on the biliary tract is significant. The mechanical factors incident to an incision in the upper part of the abdomen, the use of catgut, the tensile strength of which may rapidly decline, and

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1. Starr, A., and Nason, L. H.: Postoperative Rupture of Abdominal Wounds, J. A. M. A. **100**:310 (Feb. 4) 1933.

2. Fincke, cited by Horner, D. A.: Postcesarean Bursting of Abdominal Wounds, J. A. M. A. **93**:1126 (Oct. 12) 1929.

3. Meleney, F. L., and Howes, E. L.: The Disruption of Abdominal Wounds with the Protrusion of Viscera, Ann. Surg. **99**:5, 1934.

4. Eliason, E. L., and McLaughlin, C. W., Jr.: Post-Operative Wound Complications, Ann. Surg. **100**:1159, 1934.

5. Sokolov, S.: Das Aufplatzen der Bauchwunde nach Laparotomie mit Eventration bzw. Freiliegen der Eingeweide. Auf Grund eines Materials von 723 Fällen, Ergebn. d. Chir. u. Orthop. **25**:306, 1932.

allergic reactions to the suture material are probably not the only factors associated with this complication when local factors pertaining to the wound have been controlled.

Meleney and Howes,[5] in their interesting paper on this subject, stated:

> The whole problem resolved itself down to these three questions: How can the period of suture or tissue holding be prolonged? How can the reparative process be hastened? And how can an increase of disruptive force be prevented?

Colp [6] concluded:

> Wound dehiscence will never be an unavoidable surgical complication until methods are available to accurately differentiate those patients with poor reparative powers, and until means are at hand which will unfailingly promote the prompt healing of tissues in these specific cases.

We believe that we have an explanation for disruption of the wound in certain cases and a method for control.

For several years we have been interested in the effect of hypoproteinemia on the motility of the gastro-intestinal tract. During the course of these investigations it was necessary that certain abdominal operations be performed, and in a high percentage of dogs with well advanced hypoproteinemia evisceration or breakdown of the wound occurred after laparotomy. That this occurred after the same painstaking technic with silk sutures that we have used for many years is even more important.

The frequency with which patients suffering from lesions of the stomach, duodenum and biliary tract may exhibit hypoproteinemia has been commented on by other writers.[7] That the modern use of large amounts of solution of sodium chloride intravenously increases the tissue edema incident to a low level of the serum proteins is also well known.[8] In order to obtain a clearer idea of the relationship, we have studied the effect of hypoproteinemia and tissue edema on the healing of abdominal incisions in the dog.

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6. Colp, R.: Disruption of Abdominal Wounds, Ann. Surg. **99**:14, 1934.

7. (*a*) Ravdin, I. S., and Rhoads, J. E.: Certain Problems Illustrating the Importance of a Knowledge of Biochemistry by the Surgeon, S. Clin. North America **15**:85 (Feb.) 1935. (*b*) Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema, Arch. Surg. **27**:159 (July) 1933. (*c*) Mecray, P. M.; Barden, R. P., and Ravdin, I. S.: Nutritional Edema: Its Effect on the Gastric Emptying Time Before and After Gastric Operations, Surgery **1**:53, 1937. (*d*) Gunther, L., and Greenberg, D. M.: The Diffusible Calcium and Proteins of Blood Serum in Jaundice, Arch. Int. Med. **45**:983 (June) 1930.

8. Weech, A. A., and Ling, S. M.: Nutritional Edema: Observations on the Relation of the Serum Proteins to the Occurrence of Edema and to the Effect of Certain Inorganic Salts, J. Clin. Investigation **10**:869, 1931. Lepore, M. J.: Experimental Edema Produced by Plasma Protein Depletion, Proc. Soc. Exper. Biol. & Med. **29**:318, 1931. Mecray, Barden and Ravdin.[7c]

METHOD

In a previous paper we reported the type of diet which we used and the method of plasmapheresis employed in order to produce hypoproteinemia in the dog, together with the reasons for the use of this animal.[7e]

When the serum proteins were reduced to the level desired, the animal was prepared and anesthetized with ether anesthesia. An incision about 8 cm. long was made in each rectus muscle. The peritoneal cavity was always opened, and care was exercised that the incisions were of the same length and were made in exactly similar portions of the abdominal wall.

On one side the incision was closed with fine interrupted sutures of silk and on the other, with no. 1 chromic 20 day catgut the tensile strength of which had

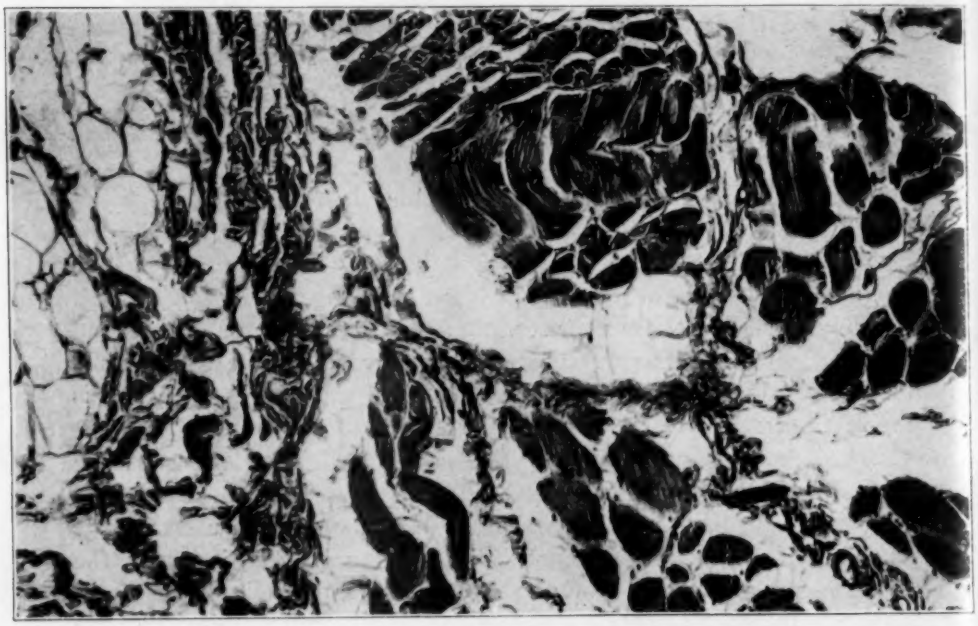

Fig. 1.—Tissue edema in a hypoproteinemic dog at the time of the abdominal incision.

previously been tested in our laboratory. The skin of each animal was sutured with silk. An exacting aseptic technic was employed on both sides, and sterile dressings and a binder were used to protect the wounds.

After operation the serum proteins were maintained at a low level, and biopsy specimens were taken from the wound on the seventh and the fourteenth postoperative day. The animals in which gross infection occurred were excluded from the study.

RESULTS

In a series of eleven dogs disruption of the wound or a failure of the wound to heal during a hypoproteinemic state was observed eight times, an incidence of 72 per cent. Tissue was removed from four of the dogs for study at intervals of seven days. In others, serious infec-

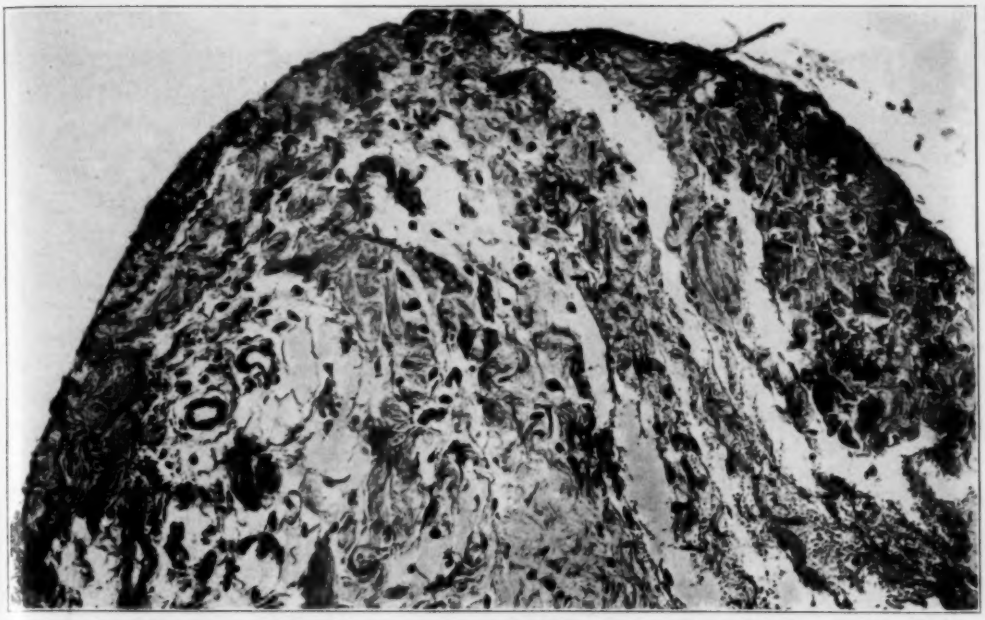

Fig. 2.—Edge of a wound in a hypoproteinemic dog seven days after operation. Tissue edema is still present. A few fibroblasts are present at the right edge of the section.

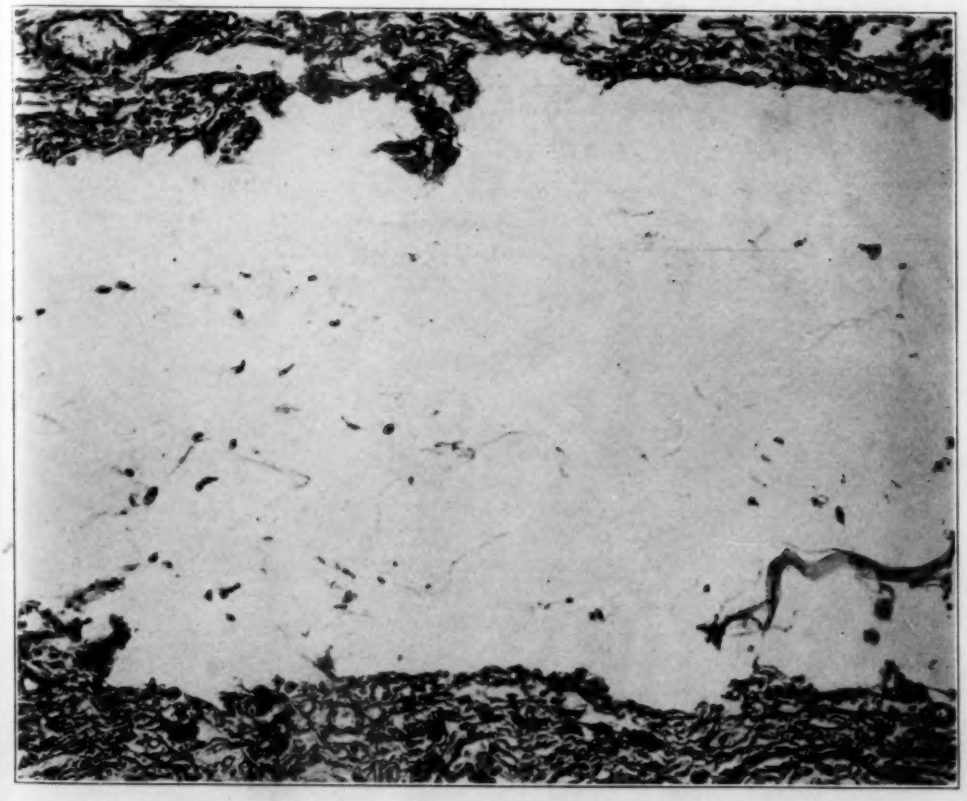

Fig. 3.—Edges of a wound of a hypoproteinemic dog seven days after operation. There is separation of the edges of the wound with a few fibroblasts in the area between the surfaces of the wound.

Fig. 4.—Area of a wound in a hypoproteinemic dog showing the presence of a catgut suture. The catgut is undergoing disintegration, and there is an extensive cellular reaction around it.

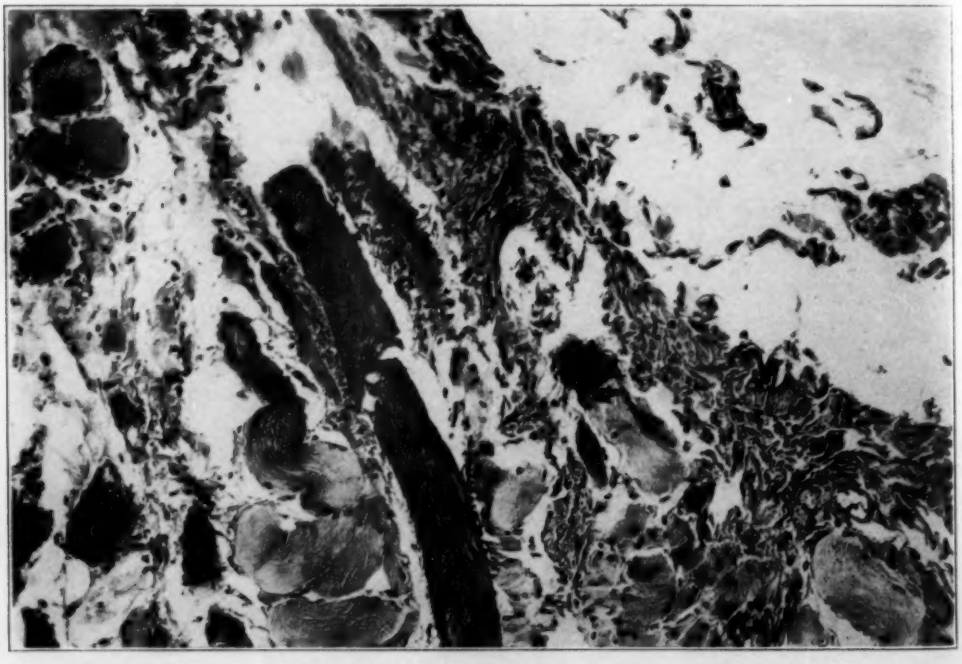

Fig. 5.—Edge of a wound in a hypoproteinemic animal fourteen days after the original incision. There is marked tissue edema. A few fibroblasts are present.

tion occurred following evisceration, resulting in a badly infected wound or in peritonitis and death.

At the time that the incisions were made the tissues were paler than normal and frequently looked as though a local anesthetic had been recently injected. At the time the first and second biopsy specimens

Fig. 6.—Edges of a wound in a hypoproteinemic dog fourteen days after operation. The edges of the wound are separated, and there is mild fibroblastic proliferation. A silk suture can be seen at the lower edge of the section. There is little cellular response to the suture.

were taken the wounds were found in four instances not to be healed, although when silk sutures were used they were frequently holding the edges together. In cutting across a wound to obtain a biopsy specimen, the tissue was found to be unhealthy looking, and serous

fluid could easily be expressed from the surfaces of the wound even as late as fourteen days after the abdominal incision was made. The tissue around the site of the incision was edematous, glistening and pale, and the bleeding was not as great as would be expected from an incision at right angles to the original incision. There was no apparent attempt at union of the wound. It seemed as though the two surfaces were merely loosely approximated by the sutures and the serous material was interposed, keeping the surfaces bathed in a solvent which prevented even the sticky adherence found in very early sterile wounds. In the wounds sutured with catgut often only the remains of the knots were found, and in some of the disrupted wounds no catgut could be found. However, in the wounds sutured with silk the sutures were present, and these loosely held the tissues together.

In the sections taken from the skin, muscle, fascia and omentum at the first operation there was an evident intercellular edema (fig. 1).

In the study of the sections taken seven and fourteen days after operation, there was little difference, except that, perhaps, the tissue edema was even more prominent. Fibroblastic proliferation was found only occasionally in the seven day sections, indicating a marked delay in fibroblastic regeneration. In the fourteen day sections fibroblasts were observed but in greatly decreased numbers (figs. 2, 3, 4, 5 and 6). The histologic picture was that of marked delay in tissue repair.

COMMENT

The part which the plasma proteins play in holding fluid in the blood vessels has been amply discussed by numerous investigators. As the colloid osmotic pressure of the plasma proteins is reduced from its normal level, fluid leaves the vessels and passes into the intercellular spaces. The addition of large amounts of solution of sodium chloride intensifies the resulting edema.

Many of the patients coming to operation for abdominal lesions have suffered from severe nutritional deficits for some time prior to operation. The accompanying dehydration, which is so often present, may mask the true level of the protein depletion, but when the dehydration is overcome the serum protein may be at or below the critical level for edema. The trauma incident to the operation increases the edema at the site of injury, and the hypoproteinemia prolongs the secondary edema of the trauma. Furthermore, the administration of large amounts of solution of sodium chloride in the postoperative period, as previously stated, intensifies the edema. Thus, several factors work hand in hand to produce a condition which is inimical to satisfactory repair of the wound.

The effect of diet on wound healing has been studied by other investigators. Clark [9] showed that on a diet high in protein there was no quiescent period in the repair of the wound in his dogs, the contraction beginning at once. In the review of Arey [10] on "Wound Repair," one is struck with the fact that many of the factors associated with repair are directly or indirectly dependent on a diet high in protein. Thus, animals fed on a diet of this type showed accelerated fibroblastic proliferation.[11] Cellular activity, on the whole, was greatly increased.[12] The quantity of secretion from the wound was decreased.[13] A diet high in carbohydrate to which alkalis have been added increased the quantity of this secretion.[13] The wounds of animals on an alkaline diet are said to be more easily infected.[14]

Thus, there are a number of factors both in the dog and in the patient who is subjected to a prolonged and serious protein deficiency which favor disruption of the wound. It has been observed that when cultures of growing cells are surrounded by an overabundance of fluid of low viscosity cell motility is retarded. Our experiments would tend to support the theory that certain of the amino-acids are essential for the stimulation of tissue growth (Osborne and Mendel,[15] Ackroyd and Hopkins [16] and Rose [17]).

We do not wish to imply that disruption of all abdominal wounds is associated with hypoproteinemia or a protein dietary deficit. A knowledge of the simplest factors in the principles of surgery would show that many factors must be taken into consideration in a discussion of the subject of wound disruption. But when all these factors have been considered and controlled, there will remain wounds whose failure to heal must be due to general, more widely acting causes. It is into

9. Clark, A. H.: The Effect of Diet on the Healing of Wounds, Bull. Johns Hopkins Hosp. **30**:117, 1919.

10. Arey, L. B.: Wound Healing, Physiol. Rev. **16**:327, 1936.

11. Harvey, S. C., and Howes, E. L.: Effect of High Protein Diet on the Velocity of Growth of Fibroblasts in the Healing Wound, Ann. Surg. **91**:641, 1930.

12. Benedict, F. G., and Carpenter, T. M.: Food Ingestion and Energy Transformations, Washington, D. C., Carnegie Institution of Washington, 1918.

13. Schade, H.; Beck, A., and Reimers, C.: Physikochemische Untersuchungen zur Wirkung der sauren Kost, Zentralbl. f. Chir. **57**:1077 (May 3) 1930.

14. Herrmannsdorfer, A.: Ueber den Einfluss der Nahrung auf die Pufferkapazität des Blutes und den Heilverlauf und Keimgehalt granulierender Wunden, Deutsche Ztschr. f. Chir. **200**:534, 1927.

15. Osborne, T. B., and Mendel, L. B.: Amino-Acids in Nutrition and Growth, J. Biol. Chem. **17**:325, 1914.

16. Ackroyd, H., and Hopkins, F. G.: Feeding Experiments with Deficiencies in the Amino-Acid Supply: Arginine and Histidine as Possible Precursors of Purines, Biochem. J. **10**:551, 1916.

17. Rose, W. C.: The Significance of the Amino Acids in Nutrition, in Harvey Lectures, 1934-1935, Baltimore, Williams & Wilkins Company, 1936, pp. 49-65.

this group that the nonhealing wounds of animals or patients with hypoproteinemia and vitamin deficiency must fall. The explanation which we have advanced concerns but one of perhaps a number of such factors which may later be shown to influence repair. Lamnan and Ingalls [18] have shown that a vitamin C deficiency may also be a factor. Hypoproteinemia is one factor, however, which can in many instances be controlled in large part in the preoperative and postoperative periods. The vomiting to which certain of these patients with hypoproteinemia are subject may be in part due to a knuckle of bowel protruding into the wound but may also be due in part to the interference with the motility of the gastro-intestinal tract which such patients exhibit. The methods of correcting the hypoproteinemia in the preoperative and postoperative periods we plan to discuss in a subsequent paper. We have corrected the hypoproteinemia by repeated transfusions and by the use of a protein hydrolysate administered by proctoclysis.

SUMMARY

We have called attention to the fact that when every other factor which we could control, except hypoproteinemia, had been controlled, disruption of the abdominal wound still occurred in a large number of dogs after abdominal incisions. Healing of the wound was greatly retarded whether silk or catgut sutures were used, but actual disruption was greater with catgut. The failure of the wound to heal was, we believe, associated with the hypoproteinemic state, a condition which is present in many patients subjected to operations on the gastric, duodenal and biliary tracts.

18. Lamnan, T. H., and Ingalls, T. H.: Vitamine C. Deficiency in Wound Healing, Ann. Surg. **105**:616, 1937.

USE OF LYOPHILE PLASMA IN CORRECTION OF HYPOPROTEINEMIA AND PREVENTION OF WOUND DISRUPTION

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AND

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Investigations of the causes of disruption of abdominal wounds have emphasized the importance of the premature absorption of catgut, improper wound closure, distention, postoperative coughing and the delayed fibroplasia so commonly encountered in this accident. It has been stated that some factor associated with the general state of the patient is important in the predisposition of the tissues to undergo the normal processes of wound repair.

That catgut loses most of its strength when exposed to tissue fluids in much less time than many reputable manufacturers give for its absorption was borne out, in both the experimental animal and man, by studies reported from this department in 1936.[1] More recently, three of us [2] found that the normal processes of wound repair could be greatly retarded by experimentally producing hypoproteinemia in the dog. That other factors are important in certain instances of wound disruption we do not doubt.

It is our purpose in this paper to establish further the relationship between hypoproteinemia and disruption of wounds by demonstrating that delay in healing of the wound in hypoproteinemic dogs may be prevented by promptly restoring the serum protein to a normal level after laparotomy and maintaining this level during the period of healing.

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1. Rhoads, J. E.; Hottenstein, H. F., and Hudson, I. F.: The Decline of the Strength of Catgut After Exposure to Living Tissues, Arch. Surg. **34**:377 (March) 1937.

2. Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: Effect of Hypoproteinemia on Wound Disruption, Arch. Surg. **36**:500 (March) 1938.

In attaining this objective we have, we believe, employed a new method, in that we have used the plasma removed by plasmapheresis, which had been lyophilized and kept in the dehydrated state until just prior to its injection. The decline in the tensile strength of catgut in the normal and the hypoproteinemic dog was studied to determine whether the disruption of wounds so often encountered in these animals in our previous study might in fact be explained by an intermediate effect of the hypoproteinemic state on absorption of catgut.

Although Clark [3] first determined that restriction of proteins in the diet resulted in prolongation of the period of healing of the wound, the probability of a relationship between protein deficiency and disruption of the wound was not realized until this complication occurred a number of times in dogs in which the serum protein had been lowered to edema levels for the study of gastric emptying following various gastric operations.[4]

Since that time, we have attempted, before and after operation on the patient, to restore the serum proteins to a more nearly normal level when a deficiency existed. Fortunately, no instance of disruption of the wound has been observed, and as the concentration of the serum protein was not determined in former instances of dehiscence, it has not been possible to demonstrate the relationship statistically in man. The frequent occurrence of rupture of a wound after operations on the stomach and biliary tract and after surgical treatment for malignant growths of the gastro-intestinal tract and the high incidence of hypoproteinemia in the same group of patients strongly suggest that such a relationship exists. In many of these patients hypoproteinemia may be masked by dehydration and may not be evident until attempts are made to restore a normal balance of fluid and electrolytes.

In the work previously reported by us, every precaution was taken not to change any condition of the control experiments other than the deficiency of protein. We had observed healing of the wound after similar operations on normal animals and had studied the processes of wound repair when no protein deficit existed.

Care was taken to supply all other known dietary factors in adequate amounts to the hypoproteinemic dogs. However, as various secondary changes conceivably might result from or in association with the hypoproteinemia, we desired to determine whether the effects previously produced could be overcome by prompt restoration of the level of serum proteins after operation. The method we have used is not technically difficult and promises to be useful clinically.

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3. Clark, Admont H.: The Effect of Diet on the Healing of Wounds, Bull. Johns Hopkins Hosp. **30**:117, 1919.

4. Mecray, P. M.; Barden, R. P., and Ravdin, I. S.: Nutritional Edema: Its Effect on the Gastric Emptying Time Before and After Gastric Operations, Surgery **1**:53, 1937.

METHOD

In a previous paper, Mecray, Barden and one of us (I. S. R.) [4] reported on the type of diet which has been used in these experiments. The frequency of plasmapheresis was increased to four times a week, in order rapidly to produce the hypoproteinemic state. The plasma so obtained was lyophilized under sterile precautions and kept for future use.

The lyophile process, as described by Mudd, Flosdorf and their associates,[5] follows:

"The serum or other biologic material to be preserved is distributed with sterile precautions into glass containers. These are immersed in a bath of Dry-Ice in a commercial solvent (methyl cellosolve [6]) at a temperature of approximately —75 C. The containers of frozen serum are attached to a manifold which leads through a condenser to a vacuum pump. The condenser is kept at —75 C. with a bath of Dry-Ice in the same solvent. The whole system is rapidly evacuated and held at a pressure of 0.05 mm. of mercury by the vacuum pump. Water vapor evaporates from the frozen serum to be trapped as ice in the condenser; the rate of evaporation is sufficient to keep the serum frozen throughout the process of desiccation. The containers are sealed without breaking the original vacuum. Storage for prolonged periods should be at refrigerator temperature. The light porous residue of serum solids quickly and completely dissolves in distilled water to regenerate a serum the potency of which is not detectably different from the original serum . . . Lyophile serum may be restored to liquid form by the addition of distilled water to one-half or even one-fourth the original volume . . . The lyophile human serum prepared by this routine and regenerated appears turbid. Examination under the darkfield microscope reveals that this turbidity is due to aggregated and coalesced lipid droplets . . . To prepare lyophile human serum for intravenous use the foregoing routine is modified. The pooled serum in large volume is processed without filtration and is then regenerated. The turbid regenerated serum is clarified by passage under two atmospheres of air pressure through a Berkefeld V filter (such a filter testing at about 6 pounds). This clarified serum is then refiltered to ensure sterility through a Berkefeld W (14 pounds) candle and is distributed into final containers and again lyophile processed."

When the serum protein was reduced to the level desired and positive roentgen evidence was obtained of marked reduction in the gastric emptying time,[4] the dog was prepared and anesthetized with ether. The operative procedures were the same as those described in the earlier paper.[2]

After operation the dogs were kept on the low protein diet, and each animal was given intravenously approximately 300 cc. of lyophile plasma daily on six days of the first week after operation and approximately 150 cc. daily on four days of the second week. Specimens for biopsy were taken from the wounds on the seventh and fourteenth postoperative days.

We studied the decline in tensile strength of catgut in the same dog before and after the induction of hypoproteinemia, using the technic described in a previous paper [1] for determination of the loss of tensile strength of catgut in tissues.

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5. Mudd, Stuart; Flosdorf, E. W.; Eagle, Harry; Stokes, J., Jr., and McGuinness, A. C.: The Preservation and Concentration of Human Serums for Clinical Use, J. A. M. A. **107**:956 (Sept. 19) 1936.

6. Methyl cellosolve is ethylene glycol monomethyl ether.

RESULTS

In three dogs subjected to bilateral laparotomy during the hypoproteinemic state, disruption of the wounds or failure to heal was not observed when the hypoproteinemia was controlled, after abdominal incision, by intravenous infusion of lyophile plasma.

At the time that the incisions were made, the tissues were paler than normal and looked as though a local anesthetic had recently been injected (fig. 1). In one dog there was approximately 1,000 cc. of ascitic fluid in the peritoneal cavity. In another the omentum was markedly edematous. The wounds at the time of the first biopsy after the abdominal incisions were somewhat drier than at the first operation, but were still moist (figs. 2 and 3). At the end of seven days the serum proteins were normal in each instance. The wounds appeared grossly to be healing normally. On the fourteenth postoperative day, at the time of the second biopsy, the wounds appeared grossly to be normally healed (figs. 4 and 5). The wounds at the time of the first and second biopsies had no similarity to those observed in hypoproteinemic dogs except moderate moistness, which was observed at the first biopsy. Considerable fibroplasia was grossly evident seven days after the abdominal incisions.

Determinations of total serum proteins gave values below the critical level for edema at the time of the original laparotomy and were elevated to within normal limits in seven days after six venoclyses of plasma. This level was maintained or elevated for the second period of seven days with four venoclyses of plasma.

In the sections taken from the skin, muscle, fascia and omentum at the time of the original abdominal incision there was evident intercellular edema (fig. 1).

In the sections taken on the seventh day some intercellular edema was still evident; however, there was definite evidence of fibroblastic proliferation and healing of the wound. The area of the newly forming scar was filled with new capillaries (figs. 2 and 3). The sections of the tissue removed on the fourteenth day revealed firm fibroblastic repair, and the intercellular edema had disappeared (figs. 4 and 5).

The mean decline in the tensile strength of no. 1 chromic catgut placed in the dog's abdominal wall for four days when the serum proteins were normal was 40.7 per cent, while the mean decline of the same type of catgut in the same dogs after developement of hypoproteinemia was 55.6 per cent. It was our impression that the animals were much more susceptible to infection at the point where the catgut protruded through the skin during the hypoproteinemic phase. It is therefore impossible to be certain whether the more rapid decline in the strength of catgut during this phase was due to this factor or to the hypoproteinemia per se.

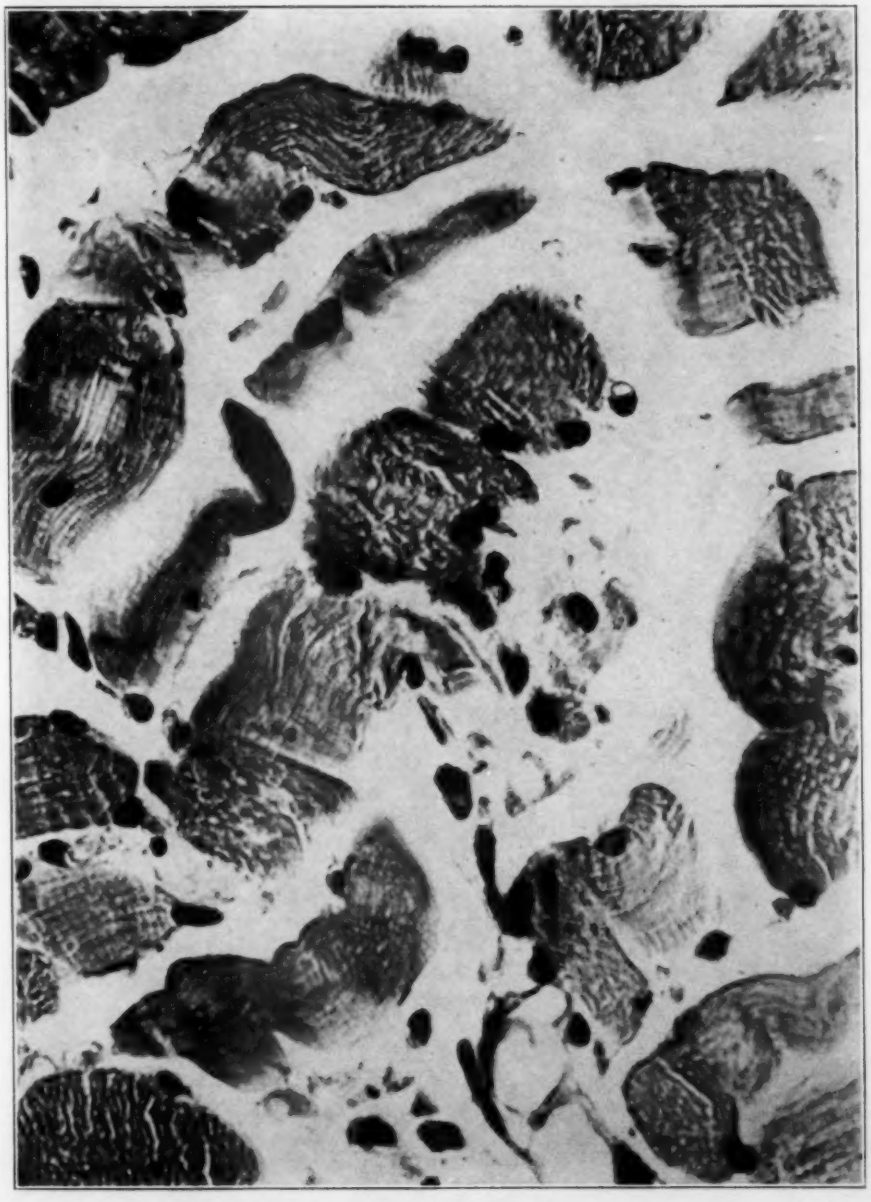

Fig. 1.—Section through the rectus muscle of a hypoproteinemic dog; × 920.

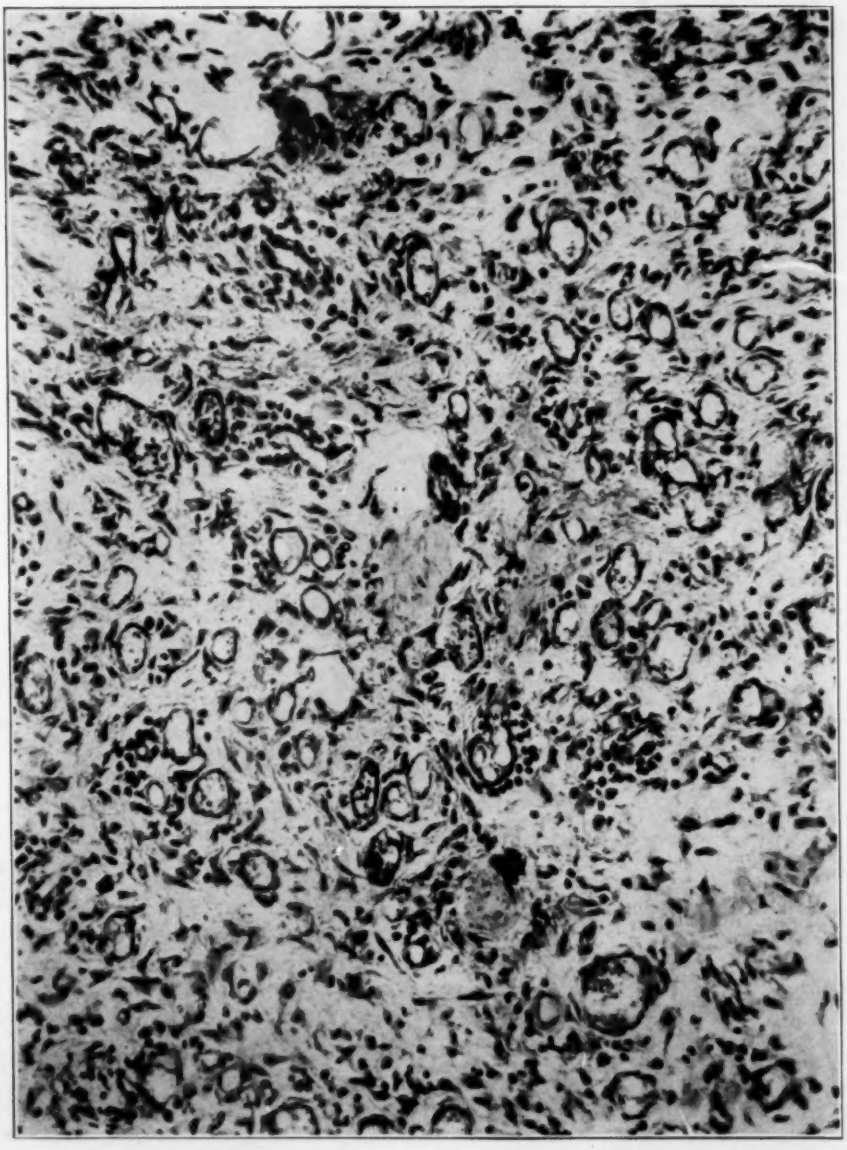

Fig. 2.—Section (× 200) through a seven day old wound, in a case in which the serum protein was normal. Many newly formed blood vessels are present. Fibroplasia is well developed. Many leukocytes are seen throughout the area.

In a former publication [2] we discussed the role of blood proteins in the production of tissue edema and the effect of diet on healing of wounds. We were led to conclude from our experiments that deficiency of blood proteins retards healing and predisposes to disruption of the wound.

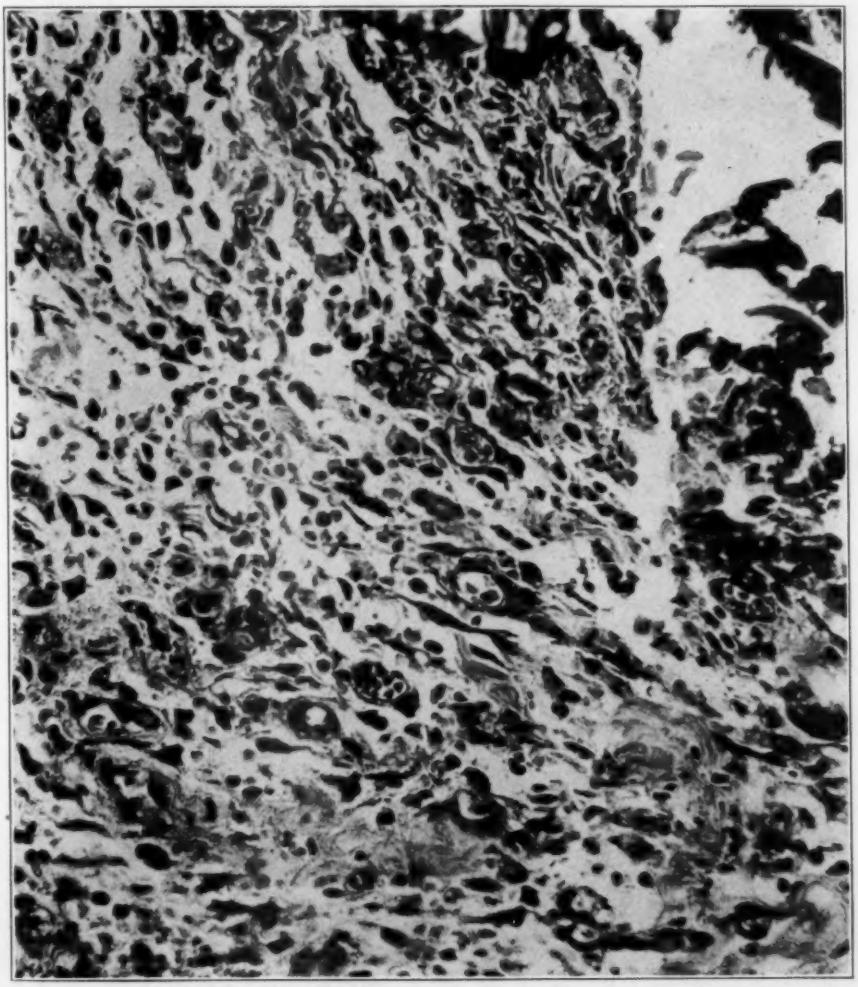

Fig. 3.—Section (× 400) through a seven day old wound. There is considerable fibroplasia in the presence of a marked leukocytic reaction. A silk suture is present in the upper right angle of the section.

The experiments reported in this paper demonstrate that healing of the wound can take place normally if the concentration of blood proteins is restored to normal and maintained there during the period that the wound is healing. We have demonstrated, furthermore, a practical

means of correcting, temporarily at least, the hypoproteinemic state. The lyophile process of preserving plasma described by Flosdorf and Mudd [7] provides plasma in such a state that it can be shipped to isolated communities and kept for months at refrigerator temperature for immediate use. In addition to these advantages, it can be given intravenously

Fig. 4.—Section (× 200) through a fourteen day old wound, showing well developed fibroplasia with excellent wound healing.

as a hypertonic solution. This has two merits: Not only does it rapidly replenish the protein deficit, but, being given as a hypertonic solution, it

7. Flosdorf, E. W., and Mudd, Stuart: Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances, J. Immunol. **29**:389, 1935.

rapidly increases the osmotic pressure of the blood, thus efficiently overcoming any tissue edema which may be present.

The interesting observation was made during this work that although the serum proteins were within normal limits, some intercellular edema

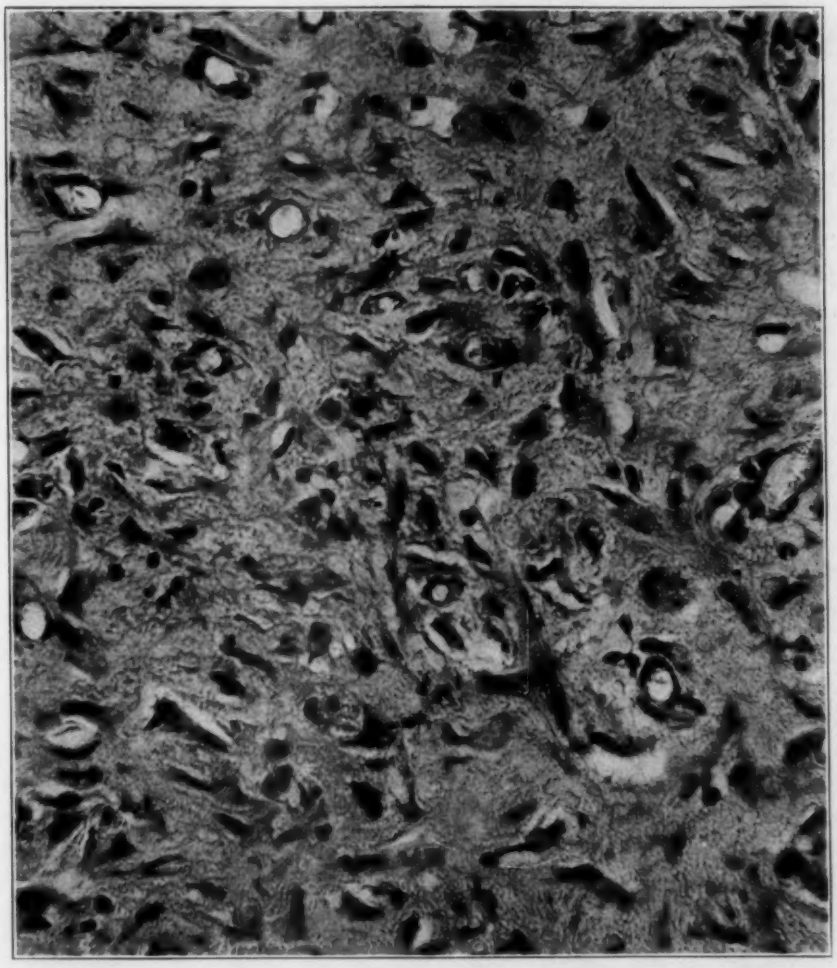

Fig. 5.—Section (× 400) through a fourteen day old wound, showing well developed fibroplasia. The new capillaries are clearly visible.

along the line of incision was still evident seven days after operation. This edema was probably associated with the trauma of operation. Nevertheless, fibroblastic repair was in progress in spite of the edema, indicating that, at least in these dogs, the edema per se did not inhibit repair of the wound.

From the results of our experiments with catgut, which showed that decrease in the tensile strength of the catgut increases with the degree of hypoproteinemia, it seems advisable to use a nonabsorbable suture material in cases of protein deficiency. If this is inadvisable because of fear of infection, the layer sutures of catgut should be reenforced by stay sutures of nonabsorbable material.

SUMMARY

1. Retardation in healing of wounds associated with hypoproteinemia in dogs may be averted by restoration of the serum protein to normal levels immediately after operation.

2. The decline in tensile strength of catgut in dogs was accelerated by induction of hypoproteinemia, although this may have been due in part to the greater tendency to infection at the junction of the skin and catgut.

3. The advantages of lyophilized serum or plasma for restoring the concentration of the blood proteins are pointed out, and the practicability of the method is demonstrated for dogs.

ILIOPECTINEAL BURSITIS

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The syndrome of iliopectineal bursitis may be overlooked easily in making a differential diagnosis of lesions of the hip joint if its likelihood is not kept in mind. This point is well illustrated by the occurrence of a large tumor mass in the right groin of an elderly man. Competent internists, surgeons and orthopedists examined the mass and made several diagnoses, but iliopectineal bursitis was not mentioned, even indirectly. As a matter of fact, the correct diagnosis was established by operation and by a study of the literature, which confirmed my opinion that this disease has not received the clinical attention that it deserves.

REPORT OF A CASE

T. L. was first seen in the orthopedic outpatient clinic in December 1926 at the age of 49. The history and symptoms were fairly typical of slowly progressive hypertrophic arthritis involving many joints over a period of years; the right hip joint was especially troublesome. During the examination a swelling the size of a lemon was noted in the right inguinal region. According to the patient, it had been present for twenty years (since 1906), developing two years after he had been kicked by a horse. There had been a short period of pain following the trauma, but the swelling itself had been painless thereafter. However, he was aware of some radiation of pain in the anterior part of the hip joint when the arthritis was more severe.

For nine years nothing further was heard from the patient. When he returned in November 1935 he stated that he had been in poor health for about one year. He could walk with great difficulty in a stooped position but preferred to stay in bed or in a wheel chair. He had been losing considerable weight and had a persistent irritating cough. He said that the mass in the right groin had reached the size of a grapefruit in 1934 and had grown somewhat larger since then.

On physical examination he presented an advanced Bechterew type of spondylitis deformans. Both hips were contracted 35 degrees in flexion. In the right groin a firm semisolid tumor, the size of a large grapefruit, elevated and displaced the femoral sheath and its contents medially. The overlying skin was streaked by a number of thin blue veins but was not adherent to the tumor beneath (fig. 1).

Roentgenograms confirmed the diagnosis of arthritis of the spine and hips. The tumor in the groin cast a slight soft tissue shadow only. Roentgenograms of the chest showed pulmonary areas which might be interpreted as circumscribed lesions. The laboratory findings were as follows: blood pressure, 136 systolic and

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Read before the Chicago Orthopedic Society, Chicago, Dec. 11, 1936. The material for this paper was obtained from the files of the Department of Orthopedic Surgery, Children's Hospital, Iowa City, service of Dr. Arthur Steindler.

90 diastolic; hemoglobin content, 53 per cent; red blood cells, 2,600,000; white blood cells, 7,800, with a normal differential count; Kahn and Wassermann reactions negative, and urine, normal.

On the basis of the large tumor mass, which had recently enlarged, the loss of weight, the secondary anemia, the cachectic appearance of the patient, the persistent cough and the suggestive pulmonary lesions, the diagnosis considered most likely was fascial sarcoma of the right inguinal region with metastases to the lung. This diagnosis was practically discarded a few days later when the tumor was aspirated and 210 cc. of clear, viscid yellow fluid was drawn off. The tumor refilled within ten days. Culture of the fluid was sterile. A guinea-pig inoculated with the fluid was killed after six weeks; no pathologic changes were found at autopsy.

In view of these findings, an exploratory operation was performed on Feb. 7, 1936, just thirty years after the tumor was first noted. A 1 per cent solution of procaine hydrochloride was employed as a local anesthesia, and an incision was made parallel and lateral to the femoral sheath. The skin, subcutaneous tissues and thinned out layers of the sartorius and iliopsoas muscles were retracted. A firm white fibrous capsule formed the external wall of the tumor. On incision, 500 cc.

Fig. 1.—Sketch of the patient showing the enlarged right iliopectineal bursa, which fills in the pelvofemoral region; the hips are in flexion contracture.

of fluid, similar to that previously aspirated, gushed out. An elliptic portion of the roof of the wall of the tumor was resected for histologic study.

When the depths of the cavity were sponged dry, a smooth-walled, shining internal lining was exposed. In the lateral portion of the floor of the sac was a tiny valvelike flap overlying a 3 to 4 mm. opening which communicated with the hip joint. When the hip was passively moved, synovial fluid was seen to pass from the joint through the opening into the sac cavity.

The communicating tunnel and the adjacent portion of the bursal floor were resected, and the capsule was sutured tightly across the defect so as to obliterate the passage between the joint and the bursa. No attempt was made to resect the bursa, but its walls were everted and the medial fibers of the sartorius and iliopsoas muscles were anchored into the floor of the sac, furnishing a surface for adhesions and absorption. In a similar manner, the medial superficial fascial layers were anchored into the floor. The wound was then closed tightly by approximation of the superficial tissues and skin.

The histologic examination of the roof of the bursa showed a wall composed of dense fibrous tissue. The innermost lining layers were not differentiated into a definite synovial membrane but were arranged compactly in strata parallel to the surface and represented pressure layers (fig. 2). The next layers outward were

formed of looser elastic tissue with occasional infiltrating round cells. The most external layers of the wall were more or less vascular, merging into the subcutaneous tissues.

An interesting finding was the inclusion of numerous small calcified fragments in the lining layers of the bursa, with foreign body giant cells in relation to them. These calcified bodies probably represented tiny pieces of calcified cartilage or bone sand which were the product of grinding down of an osteo-arthritic joint. During motion, they were subsequently washed into the bursal sac, where they became incorporated into the fibrous tissue of the lining layers.

Sections from the floor of the sac at the site of opening into the joint were similar to those just described. In addition, however, there was a well formed,

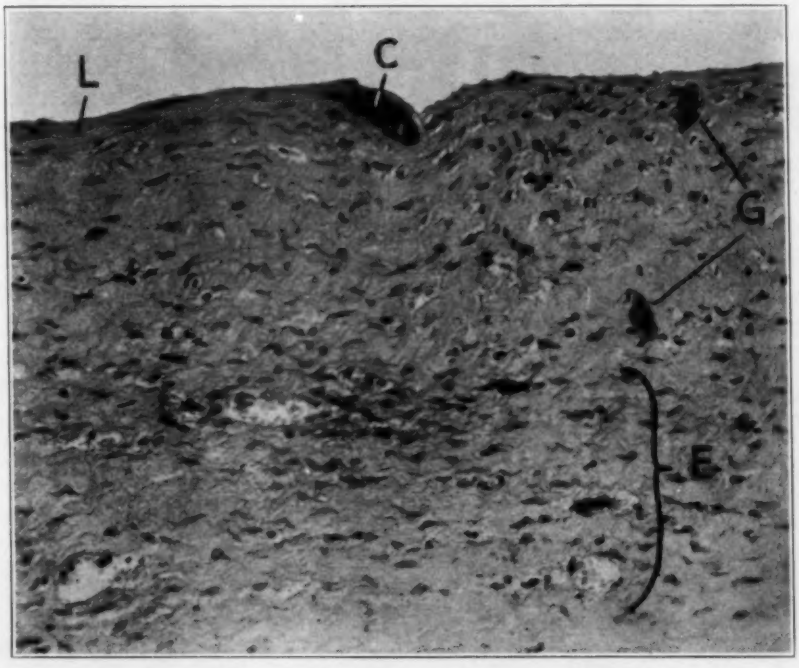

Fig. 2.—Photomicrograph of the bursa. The superficial lining of the bursa (*L*) is composed of compact fibrous tissue in parallel pressure layers, within which a small calcified body (*C*) has just been incorporated; giant cells (*G*) are seen in relation. The more external layers (*E*) are looser in structure and contain small blood vessels.

somewhat hyperplastic synovial membrane which represented the lining on the joint surface of the specimen.

Progress Notes.—The wound healed by primary intention, and the sutures were removed on the seventh day. Subsequently the patient was transferred to the medical department, where he became progressively worse due to chronic nephritis and died in uremic coma on April 22. The amyloidosis of the kidney, liver and spleen, diaphragmatic hernia, ulcerative esophagitis and pulmonary congestion and edema found at autopsy explained the confusing clinical symptoms. Exploration

of the iliopectineal bursa (two and one half months after operation) showed effective obliteration of the cavity by scar tissue. There was no sign of reestablishment of the communication with the hip joint.

ANATOMY

All anatomists [1] describe the iliopectineal bursa, although some do not designate it specifically; iliopsoas bursa and bursa mucosa subiliaca are synonyms. The iliopectineal bursa is a constant structure and is said to be the largest bursa normally present. Kessel [2] definitely demonstrated its presence in the 25.75 mm. embryo. The iliopsoas muscle covers the anterior aspect of the capsular ligament of the psoas muscle and the joint capsule. The bursa is bounded anteriorly by the iliopsoas muscle; posteriorly, by the pectineal eminence and thin portion of the capsule of the hip joint; laterally, by the iliofemoral ligament; medially, by the cotyloid ligament; above by Poupart's ligament, and below, by the pubofemoral ligament.

The anterior crural nerve lies deeply between the fleshy and the tendinous portion of the iliopsoas muscle. The femoral artery, enclosed within the crural sheath, rests on the psoas magna muscle. The femoral vein, similarly enclosed, lies between the psoas magnus and the pectineus muscle (fig. 3).

In some cases the cavity of the iliopectineal bursa is directly continuous with that of the joint. The portion of the capsule between the iliofemoral (Y) and the pubofemoral (pubocapsular) ligament is very thin, and at this point the bursa is in intimate relation with the synovial membrane of the hip joint. Either the fibrous capsule or the synovial membrane or both may be defective, permitting communication between the two cavities. Kessel found such communication in 15 per cent of 535 adult anatomic specimens. Most of these are probably congenital, but trauma or friction may also tend to establish the communication.

The bursa, when pathologically enlarged, may extend far beyond its normal confines. Durville [3] stated that its upper limit does not extend above the inguinal ligament; Lund,[4] on the contrary, said that it might

1. Buchanan, A. M.: Manual of Anatomy, Chicago, W. T. Keener & Co., 1906, vol. 1, p. 438. Cunningham, D. J.: Manual of Practical Anatomy, ed. 8, revised and edited by Arthur Robinson, Baltimore, William Wood & Company, 1927, vol. 1, p. 278. Gray, Henry: Anatomy of the Human Body, ed. 21, revised by Warren H. Lewis, Philadelphia, Lea & Febiger, 1924, p. 468. Heisler, John C.: Practical Anatomy, ed. 2, Philadelphia, J. B. Lippincott Company, 1920, p. 224. Spalteholz, Werner: Hand Atlas of Human Anatomy, ed. 4, Philadelphia, J. B. Lippincott Company, 1923, vol. 2, p. 350.

2. Kessel, F.: Ueber die Bursa mucosa iliopectinea, ihre Entwicklung und ihre Kommunikation mit der Kapsel des Hüftgelenkes, Morphol. Jahrb. **58**:413, 1927.

3. Durville, cited by Gatch and Green.[9]

4. Lund, F. B.: Iliopsoas Bursa, Boston M. & S. J. **147**:345, 1902.

extend up into the iliac fossa. It may enlarge sideways from the iliopectineal eminence to the anterior superior iliac spine. The lower border may reach into the region of the trochanter minor of the femur. On dissection, the ordinary bursa is usually large enough to admit the index finger easily for exploration of its cavity. When distended, the bursa assumes surprising dimensions (fig. 4). The bursae which are reported in the literature are usually as large as a hen's egg or a goose egg.

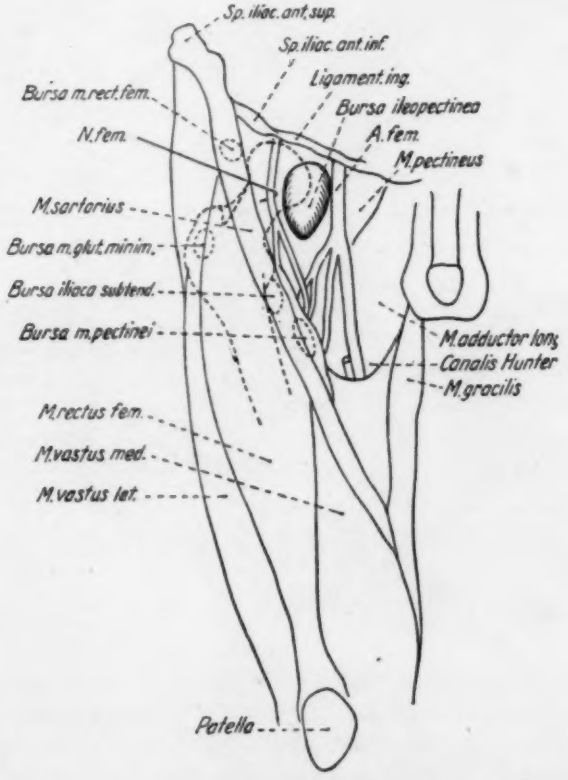

Fig. 3.—Diagram showing the relationship of the iliopectineal bursa to the other para-articular bursae, femoral nerve and vessels and femur. (From Timmermann, H. W.: Ueber die Bursitis ilio-pectinea, Med. Klin. **29**:1172 [Aug. 25] 1933.)

However, Cullen [5] reported a tumor in a male which occupied nearly one half of the pelvis and contained six large calcified cartilaginous masses. Charleston [6] described a bursa which extended from the pelvis, above Poupart's ligament, to the region of the knee joint.

5. Cullen, T. S.: A Large Cystic Tumor Developing from the Ilio-Psoas Bursa, J. A. M. A. **54**:1181 (April 9) 1910.

6. Charleston, cited by Gatch and Green.[9]

REVIEW OF THE LITERATURE

The first description of the iliopectineal bursa appears in Vesalius' "De humani corporis fabrica" written in 1555, according to Kessel.[2] However, the first clinical case of iliopectineal bursitis was reported by Fricke [7] in 1834. During the next one hundred years thirty-five additional cases were added. Zuelzer [8] in 1899 wrote a classic on the subject of iliopsoas and trochanteric bursitis, reviewing fourteen cases gathered from the literature. In 1925 Gatch and Green [9] completed a survey of twenty-four cases, including one of their own. Finally, O'Connor,[10] in an excellent treatise, demonstrated the practical application of his

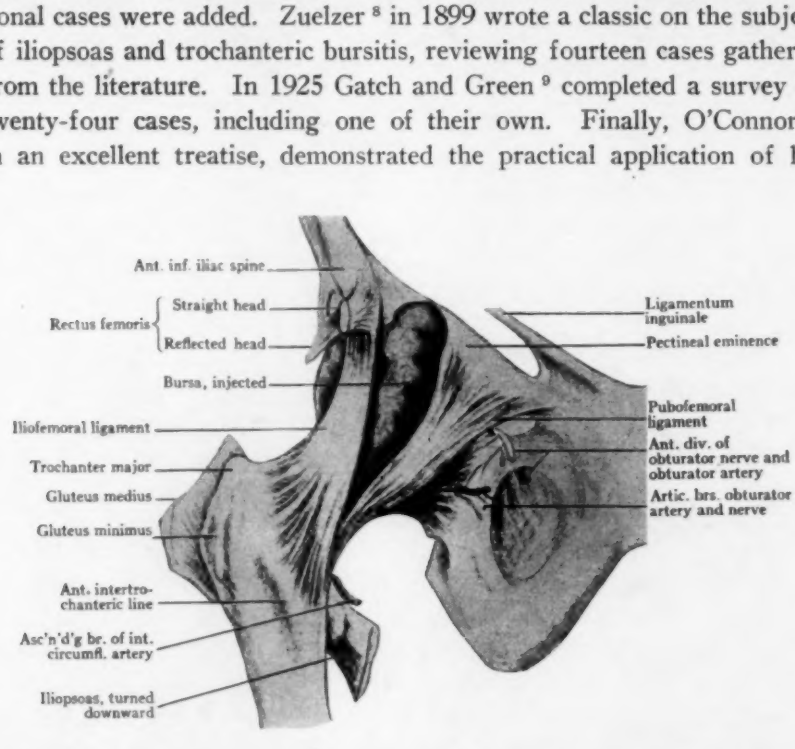

Fig. 4.—The injected iliopectineal bursa in relation to the ligamentous structures around the hip joint. (From Heisler, John C.: Practical Anatomy, ed. 2, Philadelphia, J. B. Lippincott Company, 1920, p. 224.)

experience by reporting thirty-three personal observations. The seven cases proved at operation lends credence to the accuracy of O'Connor's diagnoses in the remaining twenty-six instances.

7. Fricke, cited by O'Connor.[10]

8. Zuelzer, R.: Die Schleimbeutel der Hüfte und deren Erkrankungen, Deutsche Ztschr. f. Chir. **50**:148, 1899.

9. Gatch, W. D., and Green, W. T.: Cysts of the Ilio-Psoas Bursa, Ann. Surg. **82**:277, 1925.

10. O'Connor, D. S.: Early Recognition of Iliopectineal Bursitis, Surg., Gynec. & Obst. **57**:674, 1933.

ETIOLOGY

Earlier authors classified these bursae as simple cysts or inflammatory bursae of specific or nonspecific origin. Blood-borne infection, septicemia, gonorrhea, typhoid, syphilis and tuberculosis were considered as causative agents. However, these causes are the exception rather than the rule. I consider two factors important: arthritis and trauma, frequently in combination. Gatch and Green stated that without exception investigation in cases of a rheumatic condition disclosed a communication between the hip joint and the bursa. Therefore, it seems logical to assume that the inflammatory condition of the synovia of the joint would be mirrored in the bursal lining.

Trauma is the most important single factor in the development of iliopectineal bursitis. The male sex is therefore more often heir to this lesion than the female sex. Only three of the thirty-six cases reported up to 1935 were in women, excluding O'Connor's series in which eleven of the patients were women and twenty-two were men. Bursitis may be caused among middle-aged men performing heavy labor by multiple minute occupational injuries, the result of constant friction from the overlying psoas tendon. On the other hand, the history of trauma may be definite. A severe blow may affect the bursa directly; usually the injury is indirect, due to violent muscular activity. The mechanism consists of a sudden forceful hyperextension at the hip by a backward thrust of the body weight, frequently in the process of lifting some heavy object. As O'Connor pointed out, when the hip is flexed the iliopsoas muscle and the attached anterior portion of the bursa ride away from the joint. When the hip is suddenly hyperextended, the tension stresses which stretch the psoas muscle also stretch or traumatize the bursa.

PATHOLOGIC PICTURE

The first stage in the production of any bursitis is an inflammatory reaction to an exciting agent, whether it is toxic, chemical, mechanical or bacterial. Effusion results, and the bursa becomes distended. Rarely, hyperplastic synovitis or serositis with villi formation may develop in a bursa, but usually the bursal lining is adventitious; a true endothelial or mesothelial serous membrane has not been proved definitely. The tendency is rather for degenerative changes to take place in the superficial lining layers with the formation of a fibrin or fibrinoid substance that ultimately undergoes colliquation. The problem is still unsettled and is outside the province of this paper.

The presence of calcified foreign bodies in the bursa is interesting and represents an osteochondromatosis of the synovial bursa. This localization in the periarticular and juxta-articular bursae is much rarer

than in the articular synovia. Ardouin [11] in 1934 could find reports of only five cases in the inguinal region. Two sources of bursal bodies are possible: the bursal wall and the structures of the hip joint. The bursal wall may give rise to large bodies by a metaplastic process. Smaller bodies may result from degenerative changes in the bursal wall due to pressure. The affinity of necrotic tissue for lime salts is well known, and on this basis calcium may be precipitated in the bursal wall. In such cases the roentgenograms may possibly show an increased density in the outlines of the bursa.

When the calcified bodies originate from the structures of the hip joint, there is usually an antecedent trauma or osteo-arthritis, frequently both. Marginal lippings or exostotic spurs may chip off under stress of motion of the joint and be carried through a communicating aperture into the bursal sac, where they may enlarge by further deposition of calcium. As a rule, however, these foreign bodies are taken up by the fibrous tissue of the superficial layers of the bursal lining. This process is illustrated in my case report.

SYMPTOMS

The onset of symptoms in cases of iliopectineal bursitis due to trauma usually is acute and is characterized by rather severe pain in the groin. It is aggravated by movements of the hip, particularly extension, and is relieved by rest with the hip flexed. The involved area may show a fulness that is warm to the touch and tender to pressure. The gait is hampered by a limp. Applications of heat and rest, without weight bearing, usually alleviate the symptoms within two weeks. However, discomfort may persist if chronic bursitis develops.

In many instances iliopectineal bursitis is more insidious in its progress; it may follow some half-forgotten accident or unnoticed repeated minor occupational injury. Pain, which develops gradually, is first noticed after the fatigue of a day's labor. Later, efforts of rising from bed or from a chair evoke pain in the inguinal region. In addition to the direct pain caused by the bursitis, the patient may also complain of pain referred to the front of the knee as it radiates along the irritated femoral nerve. Timmermann [12] wrote that occasionally pain also radiates to the abdomen or the back. A limp impedes the gait because of the tendency to relax the psoas muscle by flexion of the hip. Ultimately, dragging of the extremity, limp, stumbling and weakness indicate atrophy and loss of muscle power of the psoas muscle, as O'Connor [10] observed.

11. Ardouin, G.: L'osteochondromatose des synoviales et des bourses séreuses, Rev. d'orthop. **21**:301, 1934.

12. Timmermann, H. W.: Ueber die Bursitis iliopectinea, Med. Klin. **29**:1172 (Aug. 25) 1933.

On examination, point tenderness may be elicited on pressure just below Poupart's ligament half way between the symphysis pubis and the anterior superior iliac spine (fig. 5). This site lies medial to the femoral nerve and lateral to the femoral artery. Pain is usually felt on active motion and less frequently on passive motion of the hip joint. The position of relief is assumed in flexion, external rotation and abduction.

In a significant number of cases a tumor is palpable, often visible, at the site of chronic bursitis. As a rule the tumors are quite tense, often suggesting the presence of a solid tissue neoplasm. However,

Fig. 5.—Patient with Pott's disease in the lumbar region with a large psoas abscess on the left side. For orientation, a black spot marks the site of tenderness due to iliopectineal bursitis. Compare the side view of the psoas abscess with that of the iliopectineal bursa depicted in figure 1.

O'Connor states that of ten of the cases in his series in which tumefaction was present, the swelling was fluctuant in six.

DIAGNOSIS

The diagnosis of iliopectineal bursitis may be made on the history of a direct blow in the groin or of a sudden hyperextension force at the hip. Pain develops below Poupart's ligament at a point half way between the anterior superior iliac spine and the symphysis; this spot is tender to pressure. Relief is sought by the patient's assuming the

position of flexion, external rotation and abduction. In cases in which the condition is of longer standing, a tumor is palpable. A clear fluid may be aspirated, but in the rare case of suppurative or tuberculous bursitis cloudy material with inflammatory cells and positive bacterial cultures may be found.

When a swelling is present, other lesions must be differentiated. Hernia may be ruled out by its reducibility, the transmission of the cough wave and its infrequent impediment of the motion of the joint. Tuberculosis of the spine or sacro-iliac joint explains the usual psoas abscess (fig. 5); the pea-soup pus and its bacteriologic composition confirm the diagnosis. Sworn [13] reported three cases of acute psoas abscess, from which Streptococcus haemolyticus, Staphylococcus aureus and Bacillus influenzae, respectively, were isolated. Roentgenograms of the spine and pelvis were normal. However, the acute abscess, unlike the chronic tuberculous type, tracks outward into the sheath of the iliacus muscle and seldom passes deep to Poupart's ligament into the thigh. Malignant conditions develop insidiously, the patient declines rapidly, metastases may appear and biopsy is confirmatory. Dilatation of the femoral vein, aneurysm of the femoral artery and certain types of inguinal lymphadenopathy are less common.

In the absence of swelling, osteo-arthritis should be considered. Frequently, it is concomitant with bursitis and cannot be excluded. However, the greater age of the patient, the frequent involvement of several joints, the more lateral localization of pain over the neck of the femur (Duvernay [14]), the position of deformity in flexion, external rotation and adduction and the roentgenographic picture furnish points of differentiation. Primary psoitis occurs in childhood and in adolescence (Ingelrans and Minne [15] and Klages [16]) but is seen occasionally in later life. Trauma is followed by a limp and radiating pain in the leg. Lordosis in the lumbar region increases, the inguinal lymph nodes enlarge and fever develops. A flexion, abduction and external rotation contracture develops, as in iliopectineal bursitis, but the hip joint is free. The roentgenogram may show a definitely enlarged psoas shadow. Transitory synovitis of the hip joint is essentially a disease of childhood

13. Sworn, B. R.: Acute Psoas Abscess, Brit. M. J. **2**:6 (July 1) 1933.

14. Duvernay, cited by Burckhardt, Hans: Arthritis deformans und chronische Gelenkkrankheiten, in von Bruns, P.: Neue deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1932, vol. 52, p. 362.

15. Ingelrans, P., and Minne, J.: Onze cas de psoïtis primitives observés chez des enfants et des adolescents, Rev. d'orthop. **20**:577, 1933.

16. Klages, F.: Nichttuberkulose Psoaserkrankungen im Kindesalter, Beitr. z. klin. Chir. **158**:171, 1933.

(Finder [17]). Appendicitis or ureteral calculus must be ruled out, according to Timmermann,[12] especially when the pain of iliopectineal bursitis is referred to the abdomen or back.

TREATMENT

In the early stages of bursitis the most important factor is rest in bed. Relief may be afforded by permitting flexion, but relaxation of spastic structures by simple traction with Buck's extension is preferable. Heat may hasten resolution, although occasionally cold compresses give more comfort. Aspiration relieves tension temporarily. Cure should not be expected from repeated aspirations of the larger bursae; this procedure failed in all of those cases in which it was performed.

Gatch and Green [9] stated that all authors are agreed on the excision of the chronically enlarged iliopectineal bursa. Unquestionably, total extirpation will cure the lesion, but it may require tedious, cautious dissection because of the important structures adjacent. The method of obliterating the sac worked out satisfactorily in my case. It recommends itself by virtue of its simplicity. One detail is important: any possible communication between the hip joint and the bursa must be eradicated.

COMMENT

Iliopectineal bursitis is a rather frequent lesion, but unfamiliarity with the early symptoms has undoubtedly caused the condition to be classified erroneously many times. This disease bears close resemblance to a number of conditions about the hip joint, and the differential diagnosis requires a nicety of distinction. When the bursa becomes enlarged, the lesion should be recognized without difficulty.

From the economic standpoint, it is important to diagnose the lesion in its early stages. Since bursitis often has an occupational traumatic origin, it becomes incumbent on the physician to recognize and treat the condition adequately early; to minimize its seriousness or to neglect its treatment often means the development of chronic bursitis with prolonged disability, convalescence and, not infrequently, the need for surgical intervention.

SUMMARY

The iliopectineal bursa is a constant anatomic structure, which often communicates with the hip joint.

Bursitis is frequently the result of trauma.

Iliopectineal bursitis occurs with relative frequency but goes unrecognized because its symptoms resemble those found with a number of more common lesions about the hip joint.

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17. Finder, J. G.: Transitory Synovitis of the Hip Joint in Childhood, J. A. M. A. **107**:3 (July 4) 1936.

Treatment in the early stages is conservative. With the development of an enlarged, chronically irritated bursa, surgical treatment may be necessary. The method of obliteration is successful; it is suggested in preference to the more difficult procedure of total removal of the bursa.

An unusual case of iliopectineal bursitis is reported here.

55 East Washington Street.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from page 372)

BLADDER

Tumor.—Wolfe [44] stated that routine cystoscopic examination has revealed tumor of the bladder as an occupational disease in workers exposed to benzidine, alphanaphthylamine and betanaphthylamine but not in those exposed to aniline. Analysis of the records of 2,868 routine cystoscopic examinations and of 83 cases of tumor of the bladder indicates that history and symptomatology are of little aid in diagnosis. Constant exposure to the cancerigenic agent is the important factor in the development of tumor of the bladder. Routine cystoscopic examination is the most important procedure in the medical control of the so-called aniline tumor of the bladder.

Ferguson,[45] in discussing aniline tumor of the bladder, stated that he believed that the pathogenesis of multiple papillomatosis of the bladder, both occupational and nonoccupational, is the result of the circulation, a cancerigenic agent in the blood. Because of this, he expressed the belief that the entire bladder should be treated with divided doses of

44. Wolfe, H. D.: Routine Cystoscopic Examination as a Control Measure in Anilin Tumor of the Bladder, J. Urol. **38**:216-220 (Aug.) 1937.

45. Ferguson, R. S.: Clincial Significance of the Anilin Tumor of the Bladder, J. Urol. **38**:243-250 (Aug.) 1937.

roentgen rays in order that the later appearance of new tumors in other locations may be prevented in a high percentage of cases. Application of this thesis to date has resulted in an increase in the percentage of complete regression of the primary tumors and a definite decrease in the appearance of recurrent new tumors in such cases.

Washburn [46] discussed the treatment of aniline tumor of the urinary bladder. In a group of 86 cases there were 9 deaths, a mortality of approximately 10 per cent. Twenty-four (28 per cent) of the patients had been treated too recently for a consideration of the end-results, and 53 men (62 per cent) were free from tumor. This is a creditable showing when one considers that there were 15 patients with extensive highly malignant lesions. It is to the credit of the dye industry that full responsibility has been accepted, that every facility has been provided for the discovery of early cases and that nothing has been left undone to restore the affected men to health.

Gay [47] stated that the disease produced by exposure to aniline affects the entire bladder and most frequently occurs in the lower half of the viscus above the level of the ureteral openings. The sequence of events is as follows: First, there is endothelial proliferation in focal subepithelial blood vessels. Occlusion of a vessel causes dilatation of afferent capillaries and edema of the surrounding tissue. Ectasia and proliferation of the capillaries form a mass of vessels; this mass may persist for months, or proliferation of the basal layer of the overlying epithelium may occur, with the formation of a tumor. The initial epithelial tumor may be of any degree of malignancy but tends to become more malignant with the passage of time. The sequence of vascular and epithelial lesions may be repeated indefinitely, and various stages of development as well as different grades of tumor may coexist.

Evans [48] stated, after making a study of cases of aniline tumor of the bladder, that an analysis of the literature fails to show conclusively either the carcinogenic agents or the mechanism of action in the production of such tumors. Analysis of a series of 83 cases of tumor of the bladder indicates that the tumors occur in persons who have been exposed to benzidine, betanaphthylamine, alphanaphthylamine and other nitro and amino compounds, while those exposed only to aniline have shown no tumors. The majority of the tumors appear after from six to twenty years of exposure. The average time is twelve years. The incidence of tumor is higher in persons from 40 to 60 years of age; an appreciable

46. Washburn, V. D.: The Treatment of Anilin Tumors of the Urinary Bladder, J. Urol. **38**:232-242 (Aug.) 1937.

47. Gay, D. M.: Pathology of Anilin Tumor of the Bladder, J. Urol. **38**:221-231 (Aug.) 1937.

48. Evans, E. E.: Causative Agents and Protective Measures in the Anilin Tumor of the Bladder, J. Urol. **38**:212-215 (Aug.) 1937.

number occur in those from 30 to 40 years of age. Repeated cystoscopic examinations are essential in the medical control of employees exposed to aniline, benzidine, betanaphthylamine and alphanaphthylamine. Adequate methods of control are dependent on proper methods of production, careful medical supervision and a better understanding of the mechanism of production of the tumors through research.

Leadbetter and Colston [49] reported a case of metastasis to the brain from carcinoma of the bladder and discussed 6 similar cases, reports of which were collected from the literature. Their survey of the literature indicates the rarity of cerebral metastasis from tumor of the bladder.

In an analysis of 625 reported cases of tumor of the bladder in which necropsy was performed, Leadbetter and Colston found metastasis to the brain in only 2, an incidence of only 0.3 per cent, while the incidence of metastasis in general was greater than 30 per cent. The records of the Brady Urological Institute showed that in over 800 cases of tumor of the bladder metastasis to the brain was encountered clinically only twice.

Weyerbacher and Balch [50] reported a case of leiomyosarcoma of the bladder and reviewed the literature. Reports of only 4 cases were found. The total of 5 cases comprise approximately 2 per cent of all types of sarcoma of the bladder.

Leiomyosarcoma has been found in many organs of the body other than the urinary tract. Krauskopf collected from the literature reports of 31 cases in which various organs were involved. The uterus was the seat of the lesion in 15 instances. The urinary tract appears to possess more immunity against the onslaughts of leiomyosarcoma than does the reproductive tract of the female. Besides the bladder, the only other structure of the urinary tract in which leiomyosarcoma is reported is the kidney. Leiomyosarcoma may occur during infancy or old age and may attack either the male or the female.

During the early stages these tumors manifest themselves in no way peculiar to epithelial neoplasms. Frequency, urgency and hematuria in some form or another have been present in every case. Frequency is the most prominent symptom, probably due to an associated cystitis. Straining and dribbling may occur due to mechanical obstruction of the neck of the bladder. Cystography and cystoscopy will demonstrate the tumor, if they can be successfully carried out, but it is questionable whether a mesothelial or an epithelial tumor can be correctly differentiated. If a glistening, shiny and smooth neoplasm is seen, a mesothelial neoplasm

49. Leadbetter, W. F., and Colston, J. A. C.: Brain Metastasis in Carcinoma of the Bladder, J. Urol. **38**:267-277 (Sept.) 1937.

50. Weyerbacher, A. F., and Balch, J. F.: Leiomyosarcoma of the Bladder, with Report of a Case and a Review of the Literature, J. Urol. **38**:278-287 (Sept.) 1937.

should be suspected. The surgical attack on a mesothelial tumor of the bladder differs in no way from that on an epithelial growth. Removal or destruction of the tumor in the most suitable manner adapted to the given case is the method of choice.

White and Gaines,[51] in an article on spindle cell sarcoma of the bladder, question whether all reported cases are true to type. They reported a case of sarcoma of the bladder in a man aged 38; after removal of the tumor, recurrence took place rapidly. Several sections of the growth were examined microscopically, and a diagnosis was made of transitional cell sarcoma with sarcoma-like areas. It was stated in the literature that of 69 patients with tumor of the bladder who were operated on, only 3 were considered cured; they were followed for a period of from three to twelve years. Liberal resection of the tumor-bearing wall of the bladder or complete cystectomy and urethral transplantation may result in cure in a case in which diagnosis is made early. However, only about 8 such cases have been recorded in the medical literature.

After a résumé and consideration of some practical points in the pathologic structure, symptoms and diagnosis of tumor of the bladder, Millin [52] discussed in some detail the treatment, emphasizing especially his method of endoscopic endothermic resection. The procedures available for the treatment of tumor of the bladder are:

1. High voltage roentgen treatment or distant radium treatment
2. Treatment by the urethral approach
   - (*a*) Diathermic coagulation with either the bipolar or the monopolar current
   - (*b*) Endothermic resection
   - (*c*) Introduction of radon seeds
   - (*d*) Aspiration of a bulky friable tumor (Born)
   - (*e*) Chemotherapy, consisting of the direct application of trichloracetic acid (Joseph)
   - (*f*) A combination of two or more of the foregoing methods
3. Treatment by the suprapubic approach
   - (*a*) Partial cystectomy or segmental resection
   - (*b*) Total cystectomy with implantation of the ureters in the bowel or the skin
   - (*c*) Diathermic coagulation
   - (*d*) Endothermic resection
   - (*e*) Implantation of radium
   - (*f*) Application of actual cautery
   - (*g*) Low voltage roentgen therapy direct to the tumor with the Choaul applicator
   - (*h*) Permanent cystostomy
   - (*i*) A combination of two or more of the foregoing methods

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51. White, E. W., and Gaines, R. B.: Spindle Cell Bladder Sarcoma, Surg., Gynec. & Obst. **65**:366-369 (Sept.) 1937.

52. Millin, Terence: Tumours of the Urinary Bladder with Description of a New Endoscopic Technique, Brit. J. Surg. **25**:145-171 (July) 1937.

When pain is a marked feature and uncontrolled by the appropriate use of one of these methods of treatment, a neurosurgical attack by one of the following methods may be indicated: (1) presacral neurectomy, (2) the intradural injection of alcohol or (3) lateral chordotomy.

Selection of treatment will depend on: (1) the nature of the tumor, as evidenced by the cystoscopic picture or by microscopy of sections; (2) the size of the tumor; (3) the situation of the tumor, and (4) the associated complications, either within or without the urogenital tract. In the end, personal prejudices will weigh heavily with each individual surgeon in his selection. Millin stated that the results of high voltage roentgen therapy alone are disappointing, although its use postoperatively is advised. Transurethral coagulation is the best method for accessible tumors of relatively low malignancy. However, because of the necessity of repeated séances in the treatment of large tumors and the likelihood of transplantation with repeated instrumentation, transurethral endothermic resection is an ideal method for the treatment of a large number of tumors, both benign and malignant.

Because of the limitations of the Stern-McCarthy resectoscope in removing tumors other than those situated around the orifice of the bladder, Millin has devised an operating cystoscope of convex sheath pattern with a foroblique telescope and a retrograde visual system. A number of various sized loops are used as electrodes, depending on the size of the tumor under revision. Resection is carried out as in the corresponding operation for prostatic obstruction. When the tumor is removed, the base is coagulated. Endothermic resection is contraindicated for: a tumor so situated that a relatively safe segmental resection may be done; a tumor within or about a diverticulum; an extensive growth which needs suprapubic section, as does a growth associated with prostatic obstruction when the gland is large; a tumor that is vascular and bleeds readily on urethral instrumentation, and a tumor on the anterior surface about the orifice of the bladder.

Most British urologists have largely dispensed with the use of radium in treating tumors of the bladder. Their present position in regard to the use of radium, either the element or its emanation, may be summed up by saying that it is not required in treating papillary growths; the results, both immediate and remote, are superior with partial cystectomy, electrocoagulation or endothermic resection. Inoperable infiltrating carcinomas are not cured with radium.

Cade's technic, consisting in a skilfully applied barrage of needles, with screening of from 0.8 to 1 mm. of platinum, left in situ for ten days, does cause marked regression of some radiosensitive tumors. Burns following inadequate screening may cause an intolerable cystalgia and urinary frequency.

On the basis of the results of treatment in 172 cases of vesical tumor, Millin concluded that the prognosis in cases of solitary papilloma is relatively good. With transurethral diathermic treatment, 65 per cent of the patients were free from recurrence at the end of three years. He considered the prognosis in cases of multiple papillomas to be grave. Only 4 patients were free from recurrences three years after diathermic destruction of multiple tumors.

The results following open operation for papillomas are disappointing. The outlook with endoscopic endothermic resection is much better.

Pfahler [53] stated that only about a fourth of the patients who have carcinoma of the bladder can be treated surgically without interference with the urethra or ureters; therefore, three fourths of the patients should be treated by irradiation. Treatment with highly filtered high voltage roentgen rays seems to accomplish more satisfactory results than other methods, especially in the inoperable group of tumors. This treatment involves less suffering and less interference with the daily habits of the patient than any other form of treatment. An insufficient number of patients have been treated by this method to make statistics of any value, but Pfahler estimated that one may expect disappearance of the tumor in from 30 to 50 per cent of cases.

After irradiation there is generally a cessation of hematuria at the end of three or four weeks. This does not indicate, however, that the disease has disappeared.

Cystitis is likely to be a complication before, during and after the roentgen therapy and must be dealt with just as cystitis would be treated under any other conditions. Anemia must be counteracted.

Pfahler aims to give the planned treatment within a month, which means from 20 to 25 treatments, but this number may have to be doubled or tripled. It is desirable to give as little treatment as will accomplish the results. The more accurately the disease is localized and the less its extent, the smaller will be the portals through which irradiation is given and the more one can conserve the normal tissues. On the other hand, if one confines treatment to too small an area, some remnant of the disease will be missed and recurrence will follow.

Mark [54] reported a case of endometriosis of the bladder in a patient whose chief complaints were hematuria, frequency, dysuria and disabling pain, these symptoms occurring with cyclic regularity and starting five months after hysterectomy. Because of the presence of endometriosis in the resected portion of the bladder, extending down to the perito-

53. Pfahler, G. E.: The Diagnosis and Treatment of Tumors of the Bladder by Means of Roentgen-Rays, Surg., Gynec. & Obst. **64**:989-994 (June) 1937.

54. Mark, E. G.: Endometriosis of the Bladder, J. Urol. **37**:799-807 (June) 1937.

neum, although this was not involved, and the absence of adhesions from the cervical stump or other pelvic structures to the bladder, this condition could be classified as "primary endometriosis" of the bladder. Mark expressed the belief, however, that viable endometrial tissue was implanted in the serosa of the bladder at the time of hysterectomy.

The great preponderance of reports of endometriosis of the bladder have come from the German clinics, where most careful observations have been carried out, both clinically and in the taking of the history. This led Mark to believe that such a finding should not be so rare as has been reported in the English and the American literature.

Shaw [55] described an operative technic for partial cystectomy, with reimplantation of the ureter into the bladder by the perineal approach, that has been performed successfully on the living subject. This procedure appears adaptable to infiltrating carcinomas limited to the base and to the orifice of the bladder that are not resectable by the suprapubic approach.

A man aged 63 was found on cystoscopic examination to have a necrotic papillary carcinoma involving the left ureteral orifice and the greater portion of the trigon and extending through the dilated internal sphincter into the prostatic urethra, almost to the level of the verumontanum.

The operation was performed with the patient under spinal anesthesia and in the perineal position. The usual inverted V incision was made, as is done in Young's radical operation for carcinoma of the prostate. The operation was carried out in the same manner as is the radical operation for carcinoma of the prostate, with the exception that the urethra was cut off in its prostatic portion instead of in its membranous portion. The pelvic fascia was separated laterally and anteriorly until the tractor could be felt through the anterior wall of the bladder. A transverse incision was then made through the wall of the bladder at its junction with the prostate, and the tractor was pulled down so as to give a complete exposure of the entire interior of the bladder. The distal edges of the cut bladder were grasped with Allis forceps and pulled downward, exposing the vas deferens on the right and the ureter and the vas deferens on the left. The left ureter was cut across flush with the external surface of the wall of the bladder, and a catgut ligature was placed through its tip. The arteries of the seminal vesicles were then ligated and divided, and the vasa deferentia were cut. The excised tissue contained all the prostate except the apex, the greater portion of the trigon, the left ureteral orifice and both seminal vesicles. Closure of

55. Shaw, E. C.: Perineal and Vaginal Cystectomy with Transplantation of the Ureters, J. Urol. **37**:850-857 (June) 1937.

the bladder was begun with a row of sutures on the left side at the point of the greatest defect, the lateral walls being brought down medially to form a new floor. This line of interrupted chromic catgut sutures was continued until the opening of the bladder had been reduced to such size that it could be attached to the cut off apex of the prostate by a circular row of sutures. Two drains were placed in the wound, and the levator ani muscles were approximated with two sutures of chromic catgut. A no. 22 French catheter was left in the bladder.

Cystoscopy was performed at intervals of three months for the first two years after the operation and annually until five years had elapsed. There was no recurrence of the tumor and no history of further urinary difficulties.

Bumpus [56] reported a series of cases of tumor of the bladder from the Los Angeles County General Hospital. Destruction with diathermy was used in 77, in 34 through the urethra and in 43 by transvesical exposure. Eleven of the patients in the former group were living from three to five years after transurethral electrocoagulation—apparent cures in 33 per cent. These figures indicate how uncertain ultimate recovery is once a diagnosis of tumor of the bladder has been made. Unquestionably, the poor final results were due in no small measure to the failure of the patients to come for reexamination.

Of the latter group of 43 patients treated transvesically, 25 had tumors of the papillary type; 16 of these patients are known to be dead and 5 were alive over three years. Of the 18 patients with infiltrating tumors, 10 are known to be dead and but 1 was alive over three years. Fourteen patients, or 35 per cent, died as a result of the operative procedure. Since there were 6 patients alive from three to five years and 24 were known to be dead, there would seem to be approximately a 25 per cent possibility of relief by this method of treatment, which is apparently as high an incidence of possible cure as is to be expected by any method of treatment now known. In the series of cases in which transvesical exposure was used the ureteral orifice was included 29 times in the cautery destruction, and in 10 cases the involvement of the orifice was considered a decided factor in the unsatisfactory convalescence if not a direct cause of the patient's death.

Ward [57] reported 7 cases of tumor of the bladder in which cystectomy with transplantation of the ureter was successful. Previously reported statistics have been quite unfavorable. Zukerkandle collected reports

56. Bumpus, H. C., Jr.: What We May Expect from Treatment of Bladder Tumors, California & West. Med. **47**:84-87 (Aug.) 1937.

57. Ward, Bernard: Total Cystectomy with Transplantation of the Ureters into the Pelvic Colon for Malignant Growth of the Urinary Bladder, Based on an Experience of Seven Successful Cases, Proc. Roy. Soc. Med. **30**:137-156 (Dec.) 1936.

of 64 cases from the literature, with a mortality of 50 per cent, and in 42 cases cited by Scheele the mortality for the one stage operation was 53.5 per cent. Walters operated in 76 cases of exstrophy of the bladder, in which there were 3 deaths, or a mortality of 3.9 per cent.

Ward reported 11 cases in which cystectomy was performed, with 3 deaths, or a mortality of 7 per cent. A modification of the Coffey technic of ureteral transplantation was done on 5 of Ward's patients. One lived five years, 1 a year and a half and 1 a year and nine months, and 1 died of other conditions a short time after operation. The other 2 patients had been operated on only a short time before the report was published.

Exstrophy.—Ladd and Lanman [58] presented their observations on 15 patients with exstrophy of the bladder on whom 30 ureterosigmoidostomies were performed. Methods used for treatment of exstrophy of the bladder at the Children's Hospital, in Boston, before 1930 were unsatisfactory. The operative mortality was high due to peritonitis. Postoperative renal function was often impaired to a considerable degree by infection of the urinary tract. Methods then advocated to avoid peritonitis and infection of the urinary tract and to insure urinary flow were time consuming, complicated and ill suited to the age group at the hospital. According to the authors, the chief difficulties and dangers in operative treatment of exstrophy of the bladder by uterosigmoidostomy are peritonitis that results from leakage or soiling at the site of anastomosis, obstruction of the urinary outflow at the site of anastomosis and infection of the urinary tract, with its resulting renal damage.

Experimental work on animals by Lanman and Colby from 1928 to 1930 demonstrated that if each ureter was transplanted separately any possible slight temporary impairment of urinary outflow through the side anastomosed was safely compensated for by the opposite side. Immediate postoperative peritonitis was more common when some mechanical guide through the site of the anastomosis was used, and postmortem examinations seemed to indicate that this foreign body was often a causative factor. Moreover, postmortem examinations at a later date on animals that survived showed, both grossly and histologically, that there was more infection of the urinary tract when a guide was used than when it was not. It seemed clear that if the two stage operation was performed, there was no need to fear obstruction to the urinary outflow if a guide was used. It also seemed clear that the use of a guide was not only unnecessary but dangerous. It was concluded, therefore, that the two stage operation, without the use of catheters or guides, offered the best method to minimize and prevent the dangers of peritonitis, urinary obstruction and infection of the urinary tract.

58. Ladd, W. E., and Lanman, T. H.: Exstrophy of the Bladder, New England J. Med. **216**:637-644 (April 15) 1937.

In their summary the authors stated that they considered the following principles fundamental in obviating these dangers: a two stage operation for the ureteral transplantation; transplantation of the right ureter first and of the left, from two to four weeks later; a transperitoneal approach for ureterosigmoidostomy, no catheter or guides being left but the proximal end of the ureter being opened widely by a longitudinal slit; no drainage of the peritoneal cavity; removal of the bladder as soon as is practicable after the ureteral transplantation and the selection of patients preferably between 3 and 5 years of age.

With the technic of Ladd and Lanman, the actual transplantation of the ureter is done transperitoneally, as the dangers of peritonitis are considered far less than the dangers resulting from a rather blind extraperitoneal approach. In using the extraperitoneal approach it is impossible to be sure that the ureter lies in a straight line from the kidney and that it is free from all tension and kinking. The transperitoneal approach is especially important in transplanting the left ureter, which is done from two to four weeks after transplantation of the right ureter. Intravenous pyelograms in the cases in which this technic was used showed excellent results two years after operation, especially when compared with the results following the earlier types of this operation. There were no fatalities, and good control of the bowel was obtained in every case. Ladd and Lanman advised, however, not doing the operation until the child is from 3 to 5 years of age, as by that time the patient can cooperate in acquiring control over the rectum.

Intravenous pyelograms and determinations of the blood chemistry were made with reported cases. These were normal in enough cases to lead the authors to state that preoperative infection of the urinary tract is a rarity. Later infection of the urinary tract is more likely to occur with the so-called aseptic type of extraperitoneal operation than with an operation that strives to have the course of the ureter into the bowel as straight and as unobstructed as possible.

Ulcer.—Folsom and O'Brien [59] gave a preliminary report of their observations on 7 cases of Hunner ulcer in which absolute alcohol was injected into and about the ulcers. Gas anesthesia was used for all the patients. Injections were made with a long flexible needle through the McCarthy panendoscope. From 2 to 6 cc. was injected, 0.2 cc. being introduced at each puncture. These injections were distributed about and directly into the ulcer. After the treatment the patients spent from sixteen to twenty-four hours in bed and were then able to resume their regular activities.

According to Folsom and O'Brien, definite conclusions are not warranted on the basis of their brief report in which observations were

59. Folsom, A. I., and O'Brien, H. A.: Transvesical Alcoholic Injection for Elusive Ulcer of the Bladder, J. Urol. **37**:808-814 (June) 1937.

made over such a short period of time. They were impressed, however, by the prompt relief their patients received and stated that such immediate relief can be expected in a large majority of cases. They expressed uncertainty as to the duration of the period of relief, but expressed the opinion that with added experience their injections should be more complete, thereby increasing the length of this period. Finally, they have been reassured by the lack of evidence of damage to the wall of the bladder from the alcohol. With care to prevent rupture of the bladder from overdistention, it would seem that the procedure is entirely free from danger.

Fistula.—Walters [60] presented 2 cases of recurring vesicovaginal fistulas in which successful transperitoneal repair was done. By means of his technic, each fistula is closed individually, and an omental flap is sutured between the bladder and the vagina. It would appear that such a method might be applied in the treatment of certain vesicovaginal fistulas which have heretofore been thought to be inoperable and for which ureteral transplantation to the sigmoid flexure was carried out.

Bladder Dysfunction.—Thomson-Walker [61] stated that destruction of the supralumbar portion of the spinal cord at any point is followed by disturbances of vesical function, consisting of (1) a stage of retention and (2) a stage of periodic reflex micturition. The average duration of the first stage is about fifty-five days. After some hours or days the urine begins to dribble away, the bladder remaining distended. The second stage develops gradually, and the periodic reflex contractions increase in strength until the bladder is able to empty itself completely. It has been taught that destruction of the lumbar portion of the spinal cord or of the cauda equina is followed by complete paralysis of the bladder, with overflow. However, Thomson-Walker contended that experimental and clinical evidence is to the contrary and that there is the same sequence of events in micturition as occurs in injuries of the supralumbar portion of the spinal cord.

He estimated that in the British forces during the World War the total percentage of deaths due to urinary sepsis following spinal injuries was 80. This was brought about by faulty treatment, namely, intermittent catheterization. This method cannot be too severely condemned.

Thomson-Walker discussed the problem of treatment during the first stage of distention and retention and during the stage of reflex micturition. The methods available during the first stage are: (1) noninterference, (2) expression of the contents of the bladder by pressure

60. Walters, Waltman: An Omental Flap in Transperitoneal Repair of Recurring Vesicovaginal Fistulas, Surg., Gynec. & Obst. **64**:74-75 (Jan.) 1937.

61. Thomson-Walker, John: The Treatment of the Bladder in Spinal Injuries in War, Brit. J. Urol. **9**:217-230 (Sept.) 1937.

and massage, (3) the use of an indwelling catheter and (4) early or prophylactic cystotomy.

With the first method, the bladder is allowed to distend without any local interference until overflow takes place, and eventually periodic reflex micturition develops. Although the deleterious effects of the overdistended bladder may have been overemphasized, this method is not recommended for universal adoption because of the possible effects on the musculature of the bladder and future function or on the function and structure of the kidneys; there is also a possibility of rupture of the bladder. The latter has been reported in a number of cases.

The second method consists in gentle but firm compression and massage of the distended bladder through the abdominal wall every four to six hours as soon as possible after injury, with the object of expressing its contents. It should be done early before distention becomes too marked and must be done carefully and skilfully because of the danger of rupturing the bladder. It should not be used when infection has set in.

When the indwelling urethral catheter is used, the bladder is irrigated daily; the catheter is changed twice a week and is removed when reflex micturition develops. This method is certain to produce infection, but if the bladder is kept empty it does not permit reflux and regurgitation to the upper part of the urinary tract. The disadvantages and dangers of this method are: intolerance to the catheter; periurethral infection; the expulsion or plugging of the catheter, permitting the infected bladder to become distended, and the constant supervision necessary to prevent these complications.

Thomson-Walker recommended the fourth method, or early drainage by the suprapubic route, to relieve the distended bladder until reflex urination develops. The objections to early cystotomy have been: (1) difficulty of obtaining a watertight wound, (2) possible interference with the development of automatic function and (3) cystitis, which is inevitable. These objections are groundless, because with ordinary skill the production of a watertight cystotomy wound offers no difficulties. For those to whom it does, the simplified trocar and catheter method of Mothersill and Morson is available.

Although cystitis is inevitable, infection without distention or increased intravesical pressure is not dangerous. Overdistention rather than drainage interferes with development of reflex micturition. Automatic emptying will follow no matter how long the bladder is drained. The suprapubic fistula at this stage heals without difficulty when the tube is removed. Therefore, although in some cases manual expression may be of value, the constant attention and skill necessary over long periods, the failure to empty the bladder completely in some cases and

danger of rupture would indicate that early cystotomy is the method of choice in the first stage.

Thomson-Walker discussed treatment as applied to 100 patients who had survived the wave of surgical sepsis and entered into the second stage, that of the paralyzed bladder. In 69 of these, the bladder was closed, and automaticity had been established. However, complete emptying was seldom observed because of inflammatory infiltration and consequent rigidity of the wall of the bladder from long continued sepsis. In the cases of severe infection suprapubic cystostomy with continuous irrigations with different antiseptics gave the best results. If a suprapubic fistula was present, it was enlarged and the bladder was treated in a similar method. The bladder was kept open in all cases as long as continuous drainage and washings were needed. In the case of moderately infected closed bladders mechanical washing by means of an apparatus constructed on the principles of the automatic flush was carried out for several hours daily. In addition, vaccines and all forms of urinary antiseptics were used, and the patients were encouraged to get up in wheel chairs, which improved their general condition.

Incontinence.—Godard [62] reported the successful treatment of urinary incontinence in a girl aged 6 years by the Goebell-Stoeckel procedure. The urinary incontinence had developed in association with spina bifida in the lumbosacral region accompanied by a tumor. When the child was 4 years old an operation had been performed for the spina bifida, and a soft tumor and a lipoma were removed. The incontinence had persisted, together with an insufficient control of the sphincter ani and a talipes varus on the right side. The urine dribbled away drop by drop so incessantly that the child had never experienced the urge to urinate, but on distention of the bladder with 120 cc. of water she was able to feel a slight sensation of pain. Insertion of a sound for its full length as far as it would go elicited a cry, revealing a certain slight conservation of sensitivity on the part of the bladder. A plastic operation on the neck of the bladder of the Goebell-Stoeckel type was carried out, with satisfactory results. Two small musculo-aponeurotic flaps were detached from the right and left rectus muscles, respectively, at the midline and near the umbilicus; left adherent at the bottom to the pubis, they were passed alternately, together with the pyramidalis muscle and its nerve (a branch of the twelfth intercostal nerve), behind the neck of the bladder, like a cravat, and then were brought out in front of the latter and sutured to one another with silk. This made a sort of circular pseudosphincter, suspending the neck of the bladder, the

62. Godard, Henri: Incontinence d'urine par spina bifida lombo-sacré avec tumeur traité par l'opération de Goebell-Stoeckel, J. d'urol. **43**:376-386 (April) 1937.

entire ring being bound to the pubis by the pyramidalis muscle. Suture of the abdominal wall in three planes was somewhat difficult, owing to removal of the central flaps, but was successfully carried out. The first successful attempts at urination were accomplished three weeks later, under the synergistic action of the abdominal muscles and the diaphragm. A course of reeducation was instituted, with the result that at the end of six weeks the child could remain upright for five hours without urinating and could voluntarily void 100 cc. of urine. Continence was considered satisfactory from that time on. Rather extraordinary was the fact that fecal incontinence also practically disappeared, occurring only at the time when the effort to urinate was made. No vesico-ureteral reflux was present, and the capacity of the bladder was 120 cc.

The pure hypogastric Goebell-Stoeckel technic is much better from the point of view of asepsis than the vaginal approach but is a much more delicate operation. With separation of the tissues along the neck of the bladder, hemorrhage along the perivesical plexuses is inevitable, but the procedure was accomplished without evil consequences.

In discussing this case, Gouverneur stated that incontinence of urine in cases of spina bifida is of a special kind, owing to disturbance of endovesical sensibility. It is probable in the present case that a part of the curative action must be credited to the muscular ring formed around a neck of the bladder, followed later by a ring of perivesical sclerosis, but this mechanical action was not the whole, and perhaps not even the essential, correction. It is certain that in dilacerating the perivesical and pericervical nerve plexuses one exerts action on the vesical function, and it is probably in this manner that at the same time that Godard cured his patient of urinary incontinence action was exerted on the plexuses that control the anal function, so that the rectal incontinence also disappeared almost entirely. Amelioration of rectal incontinence is proof that the Goebell-Stoeckel operation finds its true usefulness in the fact that it removes the action of the sympathetic nervous system.

Hill, Barnes and Courville [63] stated that retention of urine with distention of the bladder is a fairly common complication of resection of the rectum for carcinoma. Cellules or small diverticula, ordinarily the result of long continued obstructive or paralytic distention, may appear within two weeks. Urinary retention may be transitory or may be present for days, weeks or even months or, occasionally, may be permanent. The extent and duration of vesical dysfunction depend on the character and extent of damage to the nervous elements.

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63. Hill, M. R.; Barnes, R. W., and Courville, C. B.: Vesical Dysfunction Following Abdominoperineal Resection for Carcinoma of the Rectum, J. A. M. A. **109**:1184-1188 (Oct. 9) 1937.

The character of the urinary disturbance indicates that the parasympathetic elements are exclusively or predominantly affected. This suggests that the pelvic nerves themselves or the parasympathetic elements in the hypogastric plexuses are the seat of injury. Anatomic dissections make clear the intimate relationship between the pelvic nerves and the hypogastric plexuses and the lower part of the rectum where it penetrates the floor of the pelvis. Injuries to these nervous elements are more likely to take place when the growth involves the upper part of the rectum or the lower part of the sigmoid flexure and when there is widespread involvement of the regional lymph nodes, with fixation to other organs or tissues.

Treatment of retention by an indwelling catheter is indicated as long as there is more than 50 cc. of retained urine. If cystitis develops, which is most likely in a patient who is not catheterized, it should be appropriately treated with lavage of the bladder.

Watkins [64] reported partial retention of urine in 5 persons without obstruction or disease of the nervous system but with a markedly dilated bladder yet with perfect reflex micturition, as characterized by powerful contractions of the detrusor muscle and coordinated reflex relaxation of the urethra. He called the condition "idiopathic dilatation of the bladder" caused by overactive impulses of the sympathetic nervous system and compared it with idiopathic dilatation of the colon, or Hirschsprung's disease.

The condition described could not be classified as atony, because there were powerful contractions of the detrusor muscle. The bladder of 3 of the patients contained from 1,400 to 1,500 cc. of urine; urination proceeded with a good uninterrupted stream, yet there was from 500 to 600 cc. of residual urine. Two of the patients (females) suffered from severe constipation, the bowels acting once a week for 1 patient and once every three weeks for the other. These patients urinated only once in twenty-four hours, and then as much as from 1,200 to 1,700 cc. of urine was passed at a time.

In all of these cases roentgenographic studies of the upper part of the urinary tract showed little damage as a result of back pressure.

Three of the patients underwent presacral neurectomy, with improvement in the function of the bladder and reduction in the amount of residual urine.

Stone.—Kretschmer [65] reported a case of xanthine calculi and reviewed the literature on this type of vesical stone. The search revealed

64. Watkins, K. H.: Idiopathic Dilatation of the Bladder, Brit. J. Urol. **60**:26-35 (March) 1937.

65. Kretschmer, H. L.: Xanthin Calculi: Report of a Case and a Review of the Literature, J. Urol. **38**:183-193 (Aug.) 1937.

the presence of 15 cases on which there were sufficient data for study, and with the case reported by Kretschmer, the total is brought up to 16. The youngest patient was 4 years old, and the oldest was 69. The largest number of cases occurred in persons between the ages of 4 and 15 years. This verifies the statements which have been made that xanthine calculi occur more frequently in young subjects. The sex distribution shows that the males predominate.

Xanthine calculi reported in the literature have varied greatly in size. Langenbeck's specimen was the size of a hen's egg and weighed 338 grains (21,903 mg.). Jaillard's specimen was 2 inches (5 cm.) in length and weighed 350 grains (22,679 mg.); Fleming's specimen was a little larger than a garden pea; the multiple stones in Israel's case totaled 2,300 mg. in weight. The opinion has been expressed by some authors that xanthine calculi are found more frequently in the bladder than at other sites in the urinary tract. In none of the cases in this series was the stone found in the ureter. In 8 cases the stone was found in the bladder; in 3, in the kidney, and in 1, in the urethra. In 4 cases the location was not stated.

In Kretschmer's case roentgenographic examination gave evidence of stone in the bladder, and the review of the cases in the literature showed that positive roentgenographic findings were reported in 3 cases.

A small amount of xanthine is found constantly in the urine and may also occur in the feces with other purine bodies. Urinary calculi composed of xanthine do not seem to present clinical features distinct from other forms of urolithiasis.

Treatment of xanthine calculi does not present any special features distinct from the treatment of urinary lithiasis in general. At present the consensus seems to stress the importance of chemical examination of urinary calculi with the application of the knowledge gained to dietary measures, to prevent the formation of new concretions after operation. In cases of uric acid and xanthine calculi many authors advise a mixed diet with a preponderance of vegetables, fats and carbohydrates—a low protein intake of a purine-free nature.

Rupture.—Cahill [66] stated that the incidence of rupture of the bladder is increasing with the increase of automobile accidents. The usual cause of rupture is external traumatism to an overfilled bladder, not uncommonly seen in persons who use alcohol constantly. In an increasing proportion of cases rupture is associated with fracture of the pelvis. Occasionally rupture is secondary to medical manipulations. Intraperitoneal ruptures are more frequent than extraperitoneal ones. The symptoms and signs are shock, abdominal pain and tenderness, with a marked

66. Cahill, G. F.: Rupture of Bladder and Urethra, Am. J. Surg. **36**:653-662 (June) 1937.

desire but inability to void. Diagnosis is best made by intravenous pyelography and cystograms showing the diffused dye outside the bladder. This procedure lessens the danger of infection. Rupture of the bladder is a major abdominal catastrophe and requires immediate surgical intervention. Closure of the tear with wide drainage and aspiration is recommended. Complications are shock, hemorrhage and infection.

The mortality has been steadily declining. A review of the literature showed a mortality of 78 per cent in a series of cases reported up to 1907. Since 1929 the mortality as reported at the Squier Clinic of the Columbia-Presbyterian Medical Center, in New York, was 30 per cent. This percentage might be still lower if rupture of the bladder could be isolated from the high percentage of general injuries with which they are associated.

The urethra may be ruptured either from within or from without. Rupture from without is the more usual and is generally due to a fall on the perineum. It frequently occurs with fracture of the pelvis. Symptoms and signs are those of pain, hemorrhage and urinary extravasation. Drainage of the extravasated area followed by repair of the urethral tear gives the best results. Use of an indwelling catheter increases the danger of infection.

CANCER OF THE PENIS

Campbell [67] stated that treatment of carcinoma of the penis is guided by the size of the growth, its depth of invasion and the presence of metastasis. Superficial growths less than 2 cm. in diameter and not associated with metastasis will regularly be cured by irradiation. Hopelessly advanced carcinoma of the penis should not be operated on. When there is no apparent metastasis, conservative amputation should be performed. In half of the cases in which metastasis is apparently present in the groin, the suspected lymphadenopathy is purely inflammatory. When metastasis is proved to have occurred, the regional lymphatics should be excised *en masse*. Operations to accomplish this are described.

URETHRAL STRICTURE

Mihalovici [68] reported that of a total of 186 persons with filiform stricture treated in the last four years, 68 underwent wide internal urethrotomy, 4 external urethrotomy, 3 resection of the urethra, 3 retrograde catheterization and 3 cystostomy (twice definitive) without any fatal results. He stated that he prefers a modification of the internal procedure with the Maisonneuve urethrotome, with its lateral sections.

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67. Campbell, M. F.: Cancer of the Penis: Surgical Treatment, Am. J. Surg. **28**:55-60 (April) 1935.

68. Mihalovici, I.: Contribution au traitement opératoire et post-opératoire des rétrécissements inflammatoires de l'urètre, J. d'urol. **43**:439-449 (May) 1937.

In the unmodified Maisonneuve procedure the two sections are not equal in depth, because they are made successively and not simultaneously. In Mihalovici's modification this inequality of the sections is overcome by making them with an instrument that has its two blades of unequal size. This produces two sections of equal depth, at the right and left of the midline. From this point on, the classic procedure is carried out, the conductor being replaced by a mandrin and a sound with a cut end of no. 20, 21 or 22 caliber being introduced. The patient retains this for three days, or in certain cases of callus or multiple strictures, from four to six days. As a rule, four days after the sound is removed dilation with bougies is begun; these are used daily, and the caliber is increased by one size each time. These are generally borne very well, and the maximum size is reached in two weeks. Mihalovici gives the name "period" to the precise interval of time elapsing between passage of the last béniqué, or bougie, and the moment when the stricture begins to contract again. This period varies for different strictures, but always remains invariable in one and the same person. The important thing is to establish this period with exactitude. With this end in view, Mihalovici proceeds as follows: After dilation has been done with a sound of the highest caliber, this sound is used again twice, at intervals of three days. After the second sitting, the patient returns in six days, then in twelve, twenty-four and forty-eight days and in two, three and four months and so on, and each time a sound of the caliber which was used last is passed. As soon as it is observed that the last sound is passed only with difficulty, the interval between sittings is diminished. Thus, if after three months sounds of smaller caliber are necessary, the period should be established at two and a half months. The patient must then present himself each time after this exact interval. Some patients have intervals of one, two or three months, but, more frequently, of four, five or six months and even up to one year. They then come to have the bougie passed once each time at the fixed term. Experience acquired during four years has taught that the period, once established, has never varied.

Patients are well satisfied with this improvement over old methods, and as a rule they come exactly on the day that marks their period. The only exceptions are patients with strictures in the anterior third of the penile urethra, who usually suffer rapid recurrence and to whom accordingly there is given a straight béniqué of suitable caliber which they pass for themselves at an interval of every two or three days.

If the stricture cannot be controlled or is complicated with fistulas, temporary or definitive cystostomy occasionally has its indications. In all other cases the dilated stricture can be maintained at the same caliber indefinitely.

TUMOR OF THE SCROTUM

Mintz [69] reported 3 cases of benign tumor of the scrotum—a fibroma of the spermatic cord, a lipoma and a hemangioma of the scrotum. In all 3 cases a preoperative diagnosis of malignant new growth was made, and operation was advised. In 1 case the scrotal tumor could not be palpated as a distinct mass from the testicle, but in the other 2 a definite plane of demarcation could be felt. No history of trauma was obtained in any of the 3 cases. The patients all gave a history of an increasing testicular mass, which was their chief complaint. In no instance did the scrotal tumors transmit light. All 3 patients were successfully operated on; 2 who were traced for several years had no further trouble.

URINARY CALCULI

Berke [70] sectioned and studied a number of urinary calculi in an effort to determine their structure.

He found that the stones studied had a framework of organic matter which usually consisted of a distinct nucleus and a peripheral structure. The exact nature and distribution of these elements varied with the type of stone. The nucleus consisted of one or several of the following elements: red blood cells, white blood cells and bacteria. The peripheral structure was usually composed of fibrinous matter, arrangement and distribution of which in some of the specimens approached the detail of bone. In other specimens the fibrinous structure was vague and poorly organized. It was probably derived from blood plasma and inflammatory exudate. In some stones varying quantities of uric acid crystals were found. They often appeared as inclusions and bore no distinct relationship to the rest of the structure. However, in others, the fibrinous network was built about the crystals, so that on solution their outlines could be seen in the organic matrix. Inclusions of epithelium were seen, but in no instance were they near the nucleus.

From his observations, Berke concluded that it is apparent that the determining factors in the formation of urinary calculi may be indicated as: inflammatory processes, not necessarily bacterial in origin, furnishing nuclear constituents and fibrin; a suitable crystalloid state of urine (overcharged solution), and retention of the formed nuclear matrix, growth of the calculus usually occurring by accretion and in rare instances by coalescence.

Systemic diseases, especially disturbances of calcium and phosphorus metabolism, pathologic conditions of the bone and foci of infection may be considered predisposing causes of urolithiasis.

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69. Mintz, E. R.: Benign Tumors of the Scrotum: Report of Three Cases, New England J. Med. **216**:557-559 (April 1) 1937.

70. Berke, J. D.: Nature of Urinary Calculi, J. Urol. **38**:118-130 (July) 1937.

Holtze [71] discussed the biologic action of the formation of urinary stone. The stability of urine in the urinary tract and its high power of dissolution are guaranteed by the low surface tension between the urine and the intact mucosa, by the presence of hydrotropic substances (urea and hippuric acid) and by content in stable colloids, which absorb comparatively insoluble substances and protect them from precipitation. Urinary calculi contain from 5 to 20 per cent of albumin as a nucleus. It is probable that primarily unstable, mucoid colloids mass together and become encrusted with salts. Urine penetrates in the albuminous mass, leaving the protecting colloids behind and causing the now unprotected, almost insoluble salts to precipitate. Stagnation of urine favors development of stones. With a few exceptions (cystinuria and hypercalcaremia) the concentration of stone-forming salts in the urine is unimportant. Elimination of calcareous salts through the kidneys is parallel with their concentration in the blood and can lead directly to the formation of stone. This occurs most commonly in cases of adenoma of the parathyroid gland.

Experimental and clinical data indicate that it is improbable that vitamin A is of importance in the prevention of stone in a mild climate. Unexplained are the following facts: regional, endemic occurrence of stone, a change in the frequency of stones in the same region over a certain period of time, the hereditary character of the condition, its preference for the male sex and its disappearance among children when they become adults.

Because of the results of experimental work on animals with diets deficient in vitamin A, Higgins [72] placed a selected group of patients who had urinary calculi on a dietary regimen aimed to meet the needs of the particular calculosis. Included in this group were: (1) those with bilateral renal calculi on whom operation was not advisable; (2) those with large renal calculus who ordinarily would require nephrectomy; (3) those with small calculus in the renal pelvis which was not producing obstruction, and (4) those with a small calculus in the calix which was not producing obstruction. Treatment was prescribed also when it was desirable (1) to prevent the formation of recurrent calculi, (2) to prevent the formation of calculi in patients who had passed stones at frequent intervals but in whom no calculus could be demonstrated roentgenographically, and (3) to prevent the formation of renal calculi in patients who had orthopedic problems.

It is important that the patient be hospitalized until he is thoroughly familiar with the intricacies of the dietary modifications and until the p_H of the urine is stabilized at the desired level. In cases of unilateral

71. Holtze, F.: Biologische Grundlagen der Konkrementbildung, Ztschr. f. Urol. **31**:334-338, 1937.

72. Higgins, C. C.: Present Status of Dietary Regimen in the Treatment of Urinary Calculi, Brit. J. Urol. **9**:36-46 (March) 1937.

stones the p_H of the urine from each kidney must be obtained, because they can vary widely, and an attempted correction based on the p_H of the urine in the bladder alone might produce results opposite from those desired.

Eighteen per cent of the bacilli which infect the urinary tract and 40 per cent of the strains of Staphylococcus albus split urea, so that regardless of the type of infection it should be determined whether the organism has this power.

The chemical contents of all stones removed surgically or passed spontaneously should be determined as an aid in dietary regulation. The majority of recurrent calculi are composed of calcium phosphate and carbonates. Therefore, shifting of the p_H level to about 5.2 will prevent precipitation of the phosphates and carbonates and will minimize recurrences. Vitamine A deficiency is more prevalent than is realized. In Higgins' recent series of patients, 63 per cent showed vitamin A deficiency by the biophotometer test. By use of the high vitamin A, acid or alkaline ash diet in addition to the routine urologic armamentarium, Higgins was able to reduce the percentage of recurrent calculi from 16.4 to 4.7 per cent.

In patients with orthopedic conditions who are confined to the recumbent position for long periods of time, urinary calculi occur often and are most frequently composed of calcium phosphate and carbonates. Therefore, in such patients alkaline urinary antiseptic and large amounts of citrus fruits and alkalis are to be avoided. The high vitamin A, acid ash diet will keep the urine at a p_H unfavorable to formation of calculi.

Seventy-nine of Higgins' patients who had been passing small stones at frequent intervals were completely relieved of their symptoms for over two years by the dietary regimen. In cases of proteus infection the p_H could not be shifted to the acid side, nor was the infection controlled by dietary measures or by medication by mouth, and the patients continued to pass stones.

In 32 patients in whom a calculus was too large to pass spontaneously, dissolution occurred following dietary treatment in every case. The alkaline ash diet was used in 3 patients with uric acid stones and in 1 with cystine calculi. An acid ash diet caused the dissolution of the phosphate and carbonate stones in the remaining 28 patients.

UROGENITAL TUBERCULOSIS

Remete [73] examined material at the Budapest urologic clinic to determine whether Lowenstein's statement that avian tuberculosis played a large part in human urogenital tuberculosis was correct. He confirmed

73. Remete, Tibor: Ueber die Rolle des Geflügeltuberkulosebacillus bei der Tuberkulose der Harn- und Geschlechtsorgane des Menschen, Ztschr. f. urol. Chir. u. Gynäk. **43**:202-207, 1937.

the statement of Vorman and Welti, from the urologic clinic in Berne, that they were unable to find a single case in which avian tuberculosis was the cause of urogenital tuberculosis in man. Remete's examination was made on 42 patients and consisted of allergic cutaneous tests, culture and inoculations in guinea pigs and cockerels.

ANESTHESIA

Stockwell and Smith [74] related their experiences with pontocain as a spinal anesthetic in 1,000 urological operations. The technic for patients weighing 135 pounds (61 Kg.) or over is as follows:

No preliminary sedatives are given except to children. The authors prefer to administer sedatives, as needed, in the operating room.

For operations on the bladder, pelvis and lower extremities the injections were made at a level of third and fourth lumbar space as follows: for operations of one hour's duration, 1.5 cc. of pontocain hydrochloride, with the aspiration of 0.5 cc. of spinal fluid, and for operations of from one to three hours' duration, from 1.75 to 2 cc. of the drug, with no aspiration of spinal fluid. The average working dose is 1.75 cc. for operations of short duration and 2 cc. for those of long duration. The injection is made at the rate of 2 cc. per minute.

The dose for patients under 135 pounds is figured as 1 cc. of a 1 per cent solution for each 100 pounds (45 Kg.) of body weight and to this is added 0.25 cc. more for prolonged operations. The maximum dose is 2 cc.

Induction is easy and rapid, with an average time of six minutes for the appearance of surgical anesthesia. Perfect anesthesia was obtained in 959 patients and partial anesthesia in 40, of which a few required additional local anesthesia or a few inhalations of nitrous oxide.

Pontocain is slightly more toxic than procaine but when skilfully used no untoward reactions have occurred. Its distinct advantages are smooth onset, perfect anesthesia for two hours and possibly longer, complete absence of depression of the blood pressure, absence of disturbing gastro-intestinal reactions, smooth recovery and total absence of neurologic sequelae. The safety of any spinal anesthesia depends most on the skill and experience of the administrator.

HYPOCHLOREMIA AND UREMIA

Török and Babics [75] checked the sodium chloride content of blood and spinal fluid in 17 patients who had true uremia. They found the chlorides either within normal limits or lowered in the blood and spinal

74. Stockwell, A. L., and Smith, C. K.: Pontocaine Spinal Anesthesia in Urology, Surg., Gynec. & Obst. **65**:389-392 (Sept.) 1937.

75. Török, Alexander, and Babics, Anton: Beiträge zur Klinik der Hypochlorämie und der echten Urämie, Ztschr. f. Urol. **31**:243-249, 1937.

fluid. Results of all other examinations of the blood were consistent with severe uremia. Vomiting and diarrhea were frequent for all patients who had a lowered sodium chloride content.

Török and Babics concluded that loss of salt through profuse diarrhea or frequent vomiting or lack of salt after prolonged use of a salt-free diet can lead to a rise in nonprotein nitrogen, even in persons who have healthy kidneys, similar to that observed in patients with uremia but easily differentiated by the patient's history and by the laboratory findings. Lowering of the freezing point of the blood does not keep pace with the increase in the nonprotein nitrogen. This increase is probably due to the loss of water, which leaves the kidneys with only a small amount of water at their disposal; they are also handicapped by circulatory disturbances due to the lowered blood pressure and are unable to excrete the nitrogenous products of the body's metabolism properly.

Hypochloremia develops even faster when the kidneys are diseased and when the patient is preuremic. In this case even a small loss of water is able to cause serious trouble. Usually in such cases true uremia is present, and hypochloremia is added to the clinical picture in the form of diarrhea, vomiting and anorexia.

URINARY ANTISEPSIS

Cook[76] reviewed the results in a group of 500 patients who were treated with mandelic acid. An average daily dose of 12 Gm. of the acid was given to each patient. Most satisfactory results were obtained by continuing this therapy for a period of from six to twelve days. If at the end of this period the urine still contained bacilli, it was found advisable to discontinue treatment for from ten to fourteen days and then subsequently to institute a second course of treatment.

Helmholz and Osterberg have demonstrated experimentally that the usual bacilli found in the urinary tract are destroyed by a 0.5 per cent solution of mandelic acid at a p_H of 5.5. A lower p_H will not require such a high concentration of the acid. It is advisable, therefore, to limit the fluid intake during the administration of mandelic acid to 1,200 cc. or less for each twenty-four hours. Mandelic acid in the form of ammonium mandelate will usually maintain the desired level of p_H without use of secondary acidifying agents. In certain cases, however, it may be necessary to administer ammonium nitrate or chloride or some other acidifying agent at the same time.

Cook reported that in more than 80 per cent of the uncomplicated cases of bacillary infection of the urinary tract the condition responded satisfactorily to this form of treatment. If the infection in the urinary

76. Cook, E. N.: Further Studies on the Use of Mandelic Acid for Infections of the Urinary Tract, Proc. Staff Meet., Mayo Clin. **12**:215-217 (April 7) 1937.

tract is complicated by chronic pyelonephritis with cicatricial changes in the pelves or calices, residual urine in the kidney or bladder, chronic prostatitis, stone and tumor, the chances of rendering the urine sterile are definitely reduced. Occasionally symptoms, such as nausea, evanescent microscopic hematuria or hyaline casts in the urine, may accompany the administration of mandelic acid. Some patients have experienced tinnitus and headaches, and rarely certain dermatologic reactions have been observed.

Braasch, in discussing Cook's paper, stated that the clinical evidence of renal irritation resulting from mandelic acid is indefinite. In 2 per cent of the cases red blood cells or a few hyaline casts were found in the urine. Gross hematuria was present in only 2 of the 500 cases. In no instance was there evidence of serious injury to normal kidneys following the administration of mandelic acid. In no case was an increase in the value for blood urea noted following the administration of the acid if the primary renal function was normal. In the presence of damaged kidneys, however, the use of mandelic acid may result in a mild temporary decrease in renal function. Braasch expressed the belief that use of this drug should be contraindicated if there is definite evidence of renal insufficiency.

Helmholz [77] conducted a series of experiments and made a preliminary report on the bactericidal power demonstrated in the urine of a patient who was taking sulfanilamide by mouth. He concluded that many of the organisms that are commonly found in cases of infection of the urinary tract fail to grow in the urine of a patient who has received an appreciable amount of sulfanilamide by mouth. Further reports on this will be forthcoming.

Buchtel and Cook [78] reported their experiences with sulfanilamide in the treatment of more than 200 patients who had infections in the urinary tract. This treatment is considered in general more dangerous than acidification of the urine and administration of mandelic acid, and the latter should therefore be used whenever it will prove effective. Mandelic acid is most successful in uncomplicated cases of bacillary infection and in infections attributable to Streptococcus faecalis.

Sulfanilamide appears to be a more potent antiseptic than mandelic acid and when used is effective in an alkaline urine and also at times in the presence of marked renal insufficiency.

Coccic infections do not respond as well to sulfanilamide as do bacillary infections; this is especially true of infections due to Str. faecalis. The authors present an analysis of results in the following conditions

77. Helmholz, H. F.: The Bactericidal Power of the Urine After the Administration of Prontylin by Mouth, Proc. Staff Meet., Mayo Clin. **12**:244-245 (April 21) 1937.

78. Buchtel, H. A., and Cook, E. N.: The Use of Sulfanilamide in Treatment of Urinary Infections, Proc. Staff Meet., Mayo Clin. **12**:444-446 (July 14) 1937.

in which sulfanilamide has proved greatly superior to any other antiseptic: prostatitis, urinary infection associated with prostatitis and gonorrhea.

So far, 93 patients with infections of this type have been treated. Eight were unable to take adequate doses of the drug, and the therapeutic results in these cases were classed as failures. There were 17 patients with prostatitis unassociated with urinary infection; after one week's treatment some reduction of the prostatitis was obtained in 7 and marked reduction of the prostatitis in 9. One patient showed no improvement while taking an adequate dose. The bacteriologic composition of the prostatic secretion of the patients who responded well to treatment was no different from that of the prostatic secretion of the patients who did not respond to therapy. Patients who had associated nonspecific urethral discharge were also relieved.

There were 45 patients with prostatitis and an associated urinary infection; in 33 a bacillary infection was present, and in 12, a coccic infection. Good results were obtained in 30 of the former and in 6 of the latter, and there was a significant reduction of the amount of prostatitis in 62 per cent of the group. The patients with proteus infections responded as well as those with infections attributable to other bacilli. Eleven of those with proteus infection had taken mandelic acid previously, 1 of whom also failed to obtain relief from the use of sulfanilamide. Buchtel and Cook have previously emphasized the prognostic value of prostatic cultures in the treatment of bacillary infection. Culture of prostatic secretion will be found to be positive in 50 per cent of cases of prostatitis in which urine is sterilized by mandelic acid. In the reported cases in which sulfanilamide was used, 24 cultures of prostatic secretion were made and only 1 was positive.

Thirty-one patients had gonorrhea; 21 were men and 10 were women. Two men still had symptoms after one week of treatment, and the results of these treatments were classed as failures. Two women still had positive cultures at the conclusion of the treatment. There were 2 cases of epididymitis, 1 of arthritis and 1 of acute salpingitis, in all of which good response occurred. Cook and Buchtel have not as yet seen any recurrences following the cessation of treatment, in spite of repeated examinations. This may be due to the method of giving the drug.

This has been a most difficult drug for which to develop a standard scheme of dosage, as individual tolerance varies immensely. Ordinarily Cook and Buchtel start with an initial dose of 60 or 80 grains (4 or 5.3 Gm.) daily. This is continued for one or two days and then is reduced. After another two days the patient is placed on a maintenance dose, which is usually 40 grains (2.6 Gm.) daily, for a maximal period of ten days. In the cases of gonorrhea, once clinical cure is accomplished a dose of 20 grains (1.3 Gm.) daily is continued for from ten to fourteen days.

The authors' results from this dose of sulfanilamide have been so superior to those obtained by a constant small daily dose that it seems justified, in spite of the fact that 15 per cent of patients cannot take it. Some of these patients can start with a small dose and gradually work up to a larger one; others will obtain good results on a small daily dose; the remainder, about 10 per cent, cannot take the drug at all. It was early noticed that less sulfanilamide could be taken by an ambulatory patient than by one who is at rest in bed. Ordinarily, only the first two to three days will have to be spent in bed; after that, the dose can be reduced. Cook and Buchtel recommended this procedure when the patient is doing poorly.

Reactions are common and may prove very serious. Lassitude, dizziness and slight headache occur almost invariably. If these are relieved by rest, the dose need not be reduced. More severe reactions necessitate reduction of the dose or cessation of the drug. To continue large doses in the face of severe headache, fever, gastro-intestinal upsets, mild cyanosis, paresthesia or other reactions is inviting disaster. If any of these symptoms are severe or if cutaneous reactions occur, administration of the drug should be permanently stopped.

It is unnecessary to produce even the mildest reaction to obtain good results. As a general rule, patients taking the largest dose will show the best results. Men can take larger doses of sulfanilamide than women, and the young, more than the aged. With increasing experience, serious reactions become increasingly rare.

DIURETICS

Keith [79] stated that the diuretic action of mercurial compounds depends on the available amount of mercury present. Organic mercurial compounds produce the most marked immediate diuresis. The action is chiefly on the kidneys. Diuresis which follows the administration of mercurial compounds is usually more satisfactory than that which follows the use of digitalis or caffeine compounds, even in cases of cardiac disease. The usual procedure is to inject intravenously 0.5 cc. of a given organic compound as an initial trial dose. If no toxic effects are evident, 2 cc. is injected every three or four days as long as there is distinct diuretic response.

Of the acid-producing salts, ammonium nitrate has the most marked diuretic effect and causes less digestive disturbance. The diuretic effects of the xanthine derivatives are not so great, so rapid or so uniform as are the effects of organic mercurial compounds. The combined use of diuretics has a distinct place in present day treatment of dropsy. The

79. Keith, N. M.: The Action and Use of Diuretics with Especial Reference to Mercurial Compounds, J. A. M. A. **107**:2047-2051 (Dec. 19) 1936.

best results are obtained when the acid-producing salts or such salts as potassium nitrate and potassium chloride are administered before the organic mercurial compound is injected intravenously.

GYNECOLOGIC DISORDERS AND DISTURBANCES OF THE URINARY TRACT

The incidence of secondary changes in the upper part of the urinary tract in association with various types of gynecologic disorders is high. Kretschmer and Kanter [80] found evidence of changes in the upper part of the urinary tract in 64.7 per cent of 51 cases. Changes were found in 65.7 per cent of the cases of fibroid tumor, in 81.9 per cent of the cases of ovarian cyst and in 25 per cent of the cases of prolapses; in the 1 case of tubo-ovarian abscess there was no change in the upper part of the urinary tract. Failure to appreciate the frequency with which these lesions occur is due to the fact that there have been no routine preoperative studies in cases in which urinary symptoms and urinary signs are not present.

After an appropriate surgical procedure, a return to normal took place in 72.5 per cent of cases. Subsequent pyelograms should be carried out in all cases in which recovery has not occurred at the time the patient is discharged from the hospital.

Ács [81] emphasized the importance of the changes in the urinary tract caused by myomas of the uterus. He found marked urologic changes in 20 per cent of his cases. These changes are caused by disturbances in the circulation of the pelvis, making the bladder and the upper part of the urinary tract easily accessible to infection. In a few cases the growth, by pressure on the urethra, the bladder or the ureters, causes dilation and urinary back pressure. Myomas, even if they are small, should be surgically removed, if they are the cause of troubles in the urinary tract. Removal of the growth causes prompt recovery from the urinary symptoms and prevents recurrence or inflammatory changes.

UROGRAPHY

Braasch and McDaniel [82] stated that apparent filling defects in the outline of the renal pelvis, renal calices and ureter are frequently seen in the course of routine excretory urography. Many of these have no

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80. Kretschmer, H. L., and Kanter, A. E.: Effect of Certain Gynecologic Lesions on the Upper Urinary Tract: A Pyelographic Study, J. A. M. A. **109**:1097-1100 (Oct. 2) 1937.

81. Ács, Niklaus: Durch Myome verursachte Veränderungen der Harnwege, Ztschr. f. urol. Chir. u. Gynäk. **43**:237-247, 1937.

82. Braasch, W. F., and McDaniel, J. Z.: Significance of Filling Defects in the Urogram, Tr. Am. A. Genito-Urin. Surgeons **29**:305-312, 1936.

clinical significance. In fact, complete visualization of the renal calices is not obtained in most cases. In some cases the filling defect may be visible in the first urogram but may disappear in subsequent urograms, or vice versa. In many excretory urograms peristalsis is so active that visualization of the renal calices or pelvis may be extremely fragmentary, which in some cases may be explained by some form of imbalance in sympathetic innervation. Further difficulty in interpretation may be caused by overlying intestinal shadows, which often simulate filling defects in the renal pelvis. That these various apparent filling defects are frequently without anatomic basis is shown by their subsequent disappearance in a retrograde urogram. On the other hand, filling defects observed in the excretory urogram, when confined to the renal pelvis or to one or two renal calices and when they persist in the retrograde urogram, may be the only urographic evidence of an organic lesion and should be regarded as important evidence. Fragmentary visualization of the renal calices in the excretory urogram may disguise an actual filling defect, and if a neoplasm is suspected, a retrograde urogram should always be made.

Filling defects of organic origin which involve the renal pelvis, renal calices and the ureter are caused by a great variety of conditions, including tumor, blood clots, lithiasis, cicatricial changes, congenital deformity, postoperative deformity, granulomas, pyelo-ureteritis cystica, air bubbles, reflex spasm and tuberculosis.

Braasch and McDaniel discussed renal tumor as a common cause of filling defects in the outline of the renal pelvis and the renal calices, which may be visualized in the urogram. Although a cortical tumor usually affects the outline of the calices more than that of the renal pelvis, it may invade the pelvic lumen to a variable degree and occasionally will obliterate it. A filling defect caused by papillary epithelioma of the renal pelvis is usually confined to the renal pelvis itself, and it is often accompanied by a variable degree of pyelectasis, which involves all the calices as well as the pelvis.

Clotted blood is a common cause of a filling defect in the renal pelvis or in the ureter. This may be confined to a small portion of the pelvis or ureter, or it may obliterate their lumen entirely. When blood clots become large and organized and cause persistent urinary obstruction, temporary dilatation of the pelvis and calices may result. Blood clots usually will cause an irregular filling defect, and the shadow produced by these clots often contains areas of variable density, which suggest vacuoles. Such filling defects may be confused easily with those caused by papillary epithelioma of the renal pelvis, which sometimes causes a similar deformity. In order to exclude the possibility that filling defects observed in the urogram might be the result of recent hematuria, urogra-

phy should be repeated at the end of a week or two, that is, after the blood clots have had time to disappear. Clots which persist after hematuria caused by a condition such as pyelitis or essential hematuria have been known to cause considerable confusion in diagnosis. Blood clots in the ureter may prevent visualization of the pelvis of the kidney in the excretory urogram.

Braasch and McDaniel mentioned that as a result of ureteral catheterization and injection of fluids into the renal pelvis a bubble of air sometimes remains, which may cause a shadow suggestive of a filling defect. Air bubbles in the renal pelvis have been described in cases in which there has not been any previous instrumentation.

An apparent filling defect in the urogram may be caused by overlapping outlines of the major calices in a bifid pelvis. The intervening space between the calices may produce a shadow suggestive of a filling defect. When in doubt in cases of this kind, another urogram should always be made at a different angle.

Filling defects in the renal pelvis are often observed in cases of renal lithiasis. The urogram is of particular clinical value in exact localization of the stone and in the identification of nonopaque renal calculi.

A primary tumor of the ureter usually causes a filling defect and a localized narrowing in the ureteral lumen, with a variable degree of pyelo-ureterectasis above or around the tumor. When the tumor is small, the deformity may be difficult to recognize. Since visualization of the ureter is often inexact in the excretory urogram, it is advisable to make a retrograde urogram in every case in which a diagnosis of ureteral neoplasm should be excluded. Ureteritis cystica, when advanced, and a granuloma may cause a filling defect in the ureteral lumen and may produce a similar deformity. The latter, if large, may be confused easily with a neoplasm. Blood clots in the ureter may cause similar confusion. Acute angulation of the ureter as the result of ureterectasis and chronic ureteritis may also cause apparent filling defects in the ureterogram. The passage of bulbous bougies usually will not reveal any actual constriction.

Although visualization of the bladder is more or less a by-product of the excretory urogram, it frequently affords data of unexpected importance. The amount and density of iodine excreted into the bladder vary in different persons. It will be sufficient in many cases to visualize any gross defect in the outline of the bladder. On several occasions filling defects in the excretory cystogram have suggested the presence of neoplasm which was not previously suspected. In others, the extent of the tumor could be inferred better than in any other way. On the other hand, incomplete filling of the bladder may give an erroneous impression of a filling defect, and other corroboratory data are usually necessary.

FEVER THERAPY

Desjardins, Popp and Stuhler [83] reviewed the results obtained by fever therapy in cases of gonococcic infection of the urethra, epididymis, prostate gland, uterus, fallopian tubes and articulations from the time this form of treatment was started until July 1, 1936. During this interval various changes in the technic of treatment have been made. By these improvements in treatment, cure was effected in 92 per cent of the cases that were reported in 1936. Between Dec. 1, 1933, and July 1, 1936, 210 patients suffering from acute or chronic gonorrheal infection were treated with fever therapy. Of this number, 41 did not complete their treatment, or treatment had to be abandoned for various reasons. This group of patients was excluded from consideration. Of the 169 patients who had a complete course of treatment, 152, or 90 per cent, were cured and have not had any further physical difficulties caused by the gonococcus. Seventeen patients, or 10 per cent, were not completely cured, but their condition was improved in varying degrees. Details regarding the technic of treatment, the type of patients subjected to treatment, the criteria for cure, the factors of importance in reducing the risk of treatment to a minimum and the symptoms resulting from fever therapy are discussed.

According to the authors, it would be contrary to fact to say that fever therapy is entirely devoid of danger. At the time of their report, 516 patients had been treated with fever therapy for various conditions, and these patients had received approximately 2,580 sessions of treatment. Of this number, 1 patient died under treatment.

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83. Desjardins, A. U.; Popp, W. C., and Stuhler, L. G.: Fever Therapy for Gonococcic Infection, M. Clin. North America **21**:885-891 (May) 1937.